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THE TREATMENT OF CARCINOMA OF THE BREAST

CALDWELL LECTURE, 1937*

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INTRODUCTORY REMARKS

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Our guests from other lands may not be aware that the American Roentgen Ray Society is the oldest association of radiologists in the western hemisphere and the second oldest in the world. Tentatively organized as "The Roentgen Society of The United States," it held its first meeting in New York City in 1900 and adopted its present title. Its roster has included the names of Eugene Caldwell, Charles Lester Leonard, Mihron Kassabian, Walter Dodd, Frederick Baetjer, and Lawrie Morrison, all of whom laid down their lives in sacrifice to the new science and art that they served so faithfully and so well.

Eugene Wilson Caldwell was born in 1870. Before he had finished his academic education he helped his friend and teacher, Professor Blake, in a successful experiment in submarine telephony for the government. A few years later Roentgen's discovery was announced. Caldwell became a roentgenologist, one of the first in New York City. Then, belatedly, he took up the study of medicine and received his degree in 1905. With his remarkably inventive turn of mind, Caldwell took keen interest in improving apparatus. He devised an efficient liquid interrupter, attempted rectification of alternating current with valve-tubes, produced a satisfactory stereo-fluoroscope, and tried earnestly to perfect photography of the screen image. With Pusey he was co-author of an early textbook on roentgen diagnosis and therapeutics. After long years of suffering from malignant disease brought on by the rays, he died in 1918. In honor of this genius, inventor, physician, pioneer roentgenologist and man among men, the Society in 1920 established the annual Caldwell Lecture.

It is particularly fitting that on this occasion the Caldwell Lecture in memory of a great pioneer is to be delivered by George Edward Pfahler, himself a distinguished pioneer, renowned American radiologist, past president of The American Roentgen Ray Society, outstanding teacher, practitioner and leader of diagnostic and therapeutic radiology on this continent. Fellow radiologists, I present to you Doctor Pfahler!

* The eighteenth Caldwell Lecture, delivered at the Thirty-eighth Annual Meeting of the American Roentgen Ray Society, in conjunction with the Fifth International Congress of Radiology, Chicago, Illinois, Sept. 13–17, 1937.

I FEEL greatly complimented in being invited by the American Roentgen Ray Society to give the annual Caldwell Lecture; first, because we all honor ourselves when we recognize the merits and perpetuate the memory of a great man who was our colleague; second, because of the lustre which has been given to this occasion by the distinguished men who have given this lecture before me, and third, because Caldwell was a great friend of mine and, in 1910, we seriously considered the formation of a partnership involving my moving to New York City. He was a leading member of the American Roentgen Ray Society, a great scientist, a sincere critic, but, best of all, a good friend to all who had the privilege of knowing him. We honor Caldwell most by following in his footsteps in the search for truth and in the advancement of our science, by working out a solution of some of our immediate problems. One of the problems which has not been solved is the treatment of carcinoma of the breast.

According to United States Vital Statistics, in 1920 there were 6,665 deaths from cancer of the breast, which had increased in 1929 to 10,204 deaths, and it has been stated that there were 13,000 in 1933. Since the average length of life before death from carcinoma of the breast is from three and a half to four years, and since probably 20 per cent of all cases are permanently cured, we have a right to assume that approximately 50,000 women in the United States have cancer of the breast at the present time. Much progress has been made in the treatment of carcinoma of the breast if one compares the present-day results with those obtained fifty years ago. At that time the operative mortality as reported from the Billroth Clinic was 23 per cent, and the three-year cures were only 4.3 per cent, while today, the operative mortality varies from less than 1 per cent to 5 per cent, and the five-year cures vary from 70 per cent in Stage I* to 23 per cent in Stage II (no longer encapsulated within the breast), and almost nil in Stage III.

* I am using the term clinical "Stage" I, II, III and IV, to distinguish them from the microscopically malignant "Grades" 1, 2, 3 and 4.

Ewing says, "From clinical and pathological studies I have drawn the impression that, in dealing with mammary cancer, surgery meets with more peculiar difficulties and uncertainties than with almost any other form of the disease. The anatomical types of the disease are so numerous, the variations in clinical course so wide, the paths of dissemination so free and diverse, the difficulties of determining the actual conditions so complex, and the sacrifice of tissue so great, as to render impossible in the majority of cases a reasonably accurate adjustment of means to ends." The great advance in the treatment of carcinoma of the breast was made in 1894, when Halsted described the present day radical operation (Fig. 1).

Since 70 per cent are cured if operated upon while the disease is strictly confined to the breast, our aim must be to see that all operations are performed while the disease is still in Stage I (small tumor strictly confined to the mammary gland). Unfortunately, only 10 per cent of the patients come to the surgeon in this early stage. To accomplish this best result, the laity must become educated as to the danger of lumps, lancinating pains and bloody discharge from the nipple. Likewise the physician must become more alert and more skilled in early diagnosis. If a woman consults us early and we fail in diagnosis, condemnation will follow. The public is now being aroused by the "American Army of Women to Fight Cancer," organized and working under the direction of the American Society for the Control of Cancer. This movement will bring patients earlier, and will undoubtedly place an increased burden and responsibility for early diagnosis upon us as physicians; and particularly upon the family physician, the surgeon and the radiologist. The difficulties in making an early diagnosis are well illustrated by a report from MacCarty. He has studied the records of 2,100 cases at the Mayo Clinic

in which a doubtful diagnosis was made in 21.5 per cent, and of these, the diagnosis was incorrect in 37.2 per cent. If such difficulties arise in a large clinic with highly trained men, the problem must be much greater for the general practitioner who sees only a few cases in a year. The radiologist must be trained as and assume the responsibility of a consultant. Some of these patients will consult the radiologist rather than the surgeon. We must not let this fear of operation influence our judgment and choose to treat a patient who can be better treated by surgery.

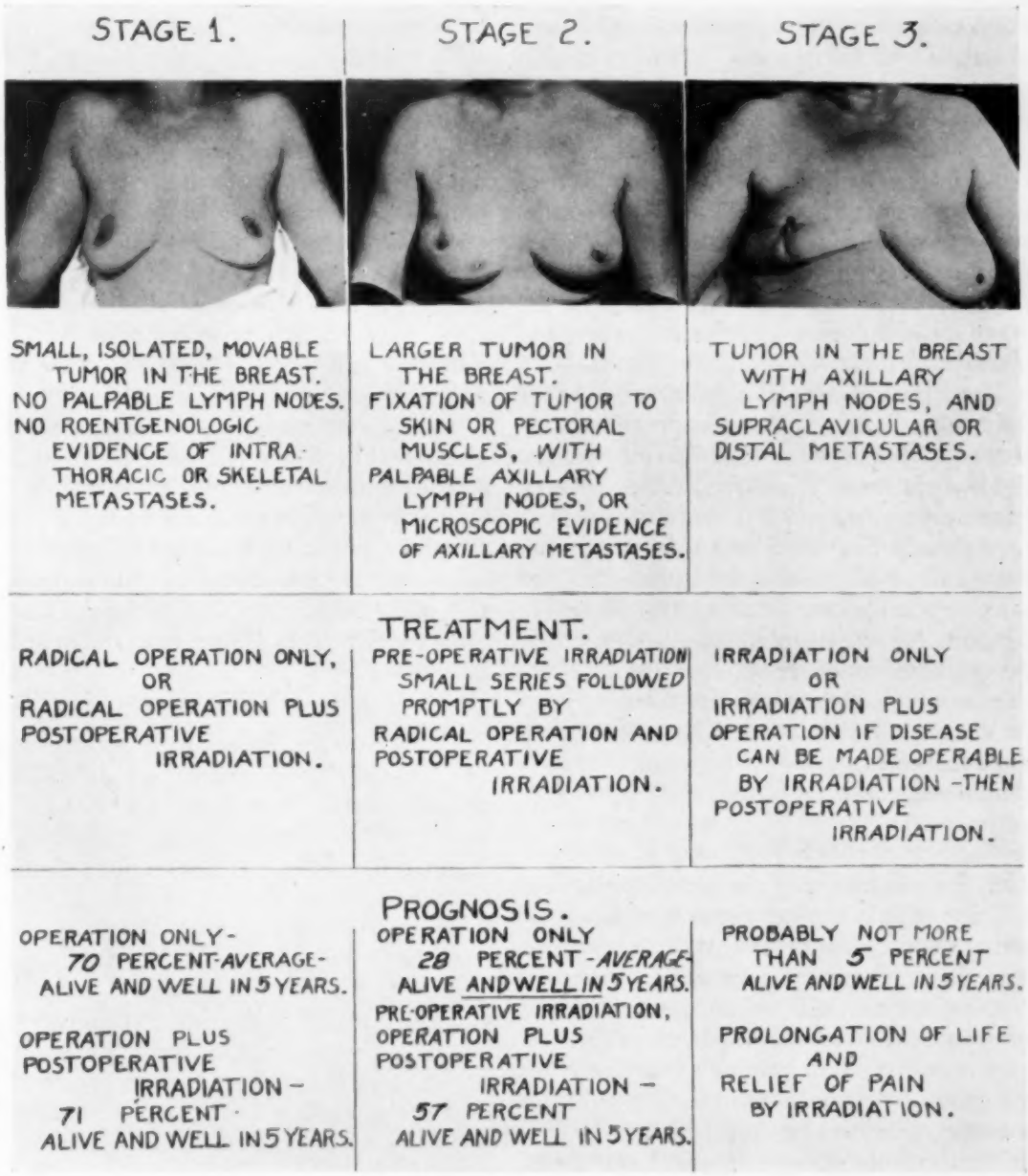
STAGE 1.
STAGE 2.
STAGE 3.
SMALL, ISOLATED, MOVABLE TUMOR IN THE BREAST. NO PALPABLE LYMPH NODES. NO ROENTGENOLOGIC EVIDENCE OF INTRA-THORACIC OR SKELETAL METASTASES.
LARGER TUMOR IN THE BREAST. FIXATION OF TUMOR TO SKIN OR PECTORAL MUSCLES, WITH PALPABLE AXILLARY LYMPH NODES, OR MICROSCOPIC EVIDENCE OF AXILLARY METASTASES.
TUMOR IN THE BREAST WITH AXILLARY LYMPH NODES, AND SUPRACLAVICULAR OR DISTAL METASTASES.
TREATMENT.
RADICAL OPERATION ONLY, OR RADICAL OPERATION PLUS POSTOPERATIVE IRRADIATION.
PRE-OPERATIVE IRRADIATION SMALL SERIES FOLLOWED PROMPTLY BY RADICAL OPERATION AND POSTOPERATIVE IRRADIATION.
IRRADIATION ONLY OR IRRADIATION PLUS OPERATION IF DISEASE CAN BE MADE OPERABLE BY IRRADIATION -THEN POSTOPERATIVE IRRADIATION.
PROGNOSIS.
OPERATION ONLY - 70 PERCENT-AVERAGE- ALIVE AND WELL IN 5 YEARS.
OPERATION PLUS POSTOPERATIVE IRRADIATION - 71 PERCENT ALIVE AND WELL IN 5 YEARS.
OPERATION ONLY 28 PERCENT - AVERAGE- ALIVE AND WELL IN 5 YEARS.
PRE-OPERATIVE IRRADIATION, OPERATION PLUS POSTOPERATIVE IRRADIATION - 57 PERCENT ALIVE AND WELL IN 5 YEARS.
PROBABLY NOT MORE THAN 5 PERCENT ALIVE AND WELL IN 5 YEARS.
PROLONGATION OF LIFE AND RELIEF OF PAIN BY IRRADIATION.

Fig. 1. This illustrates the three clinical stages of carcinoma of the breast.

We must also remember that rough and repeated examinations of the breast are dangerous (Holman). I believe that the best results in the management of cancer

of the breast will be obtained in all cases if there is a consultation between the family physician, the surgeon and the radiologist. Fortunately, the radiologist can be of some technical assistance in a roentgenographic examination of the breast, the chest and the skeleton. Ultimately, a wide excision of the tumor or a mastectomy for microscopical diagnosis may be the most conservative treatment of a doubtful case. Dawson and Tod, after an examination of a large amount of material say, "In women over 35 years, simple mastectomy with immediate examination of the gross pathology of the breast and submission of the tissue for histological opinion is the method of choice."

The operative results in carcinoma of the breast have not been appreciably improved in the past forty years (Hutchison, and Lewis and Rienhoff). The failures from surgery occur in those cases which have passed beyond Stage I, in which the disease has become attached to the skin or has extended to the axillary lymph nodes (Stage II). Stage III includes those in which the disease has extended beyond the axilla; in which the tumor tissue is fixed to the chest wall or to the axillary tissue, has invaded the skin, or in which the breast is edematous.

RECOMMENDATIONS, STAGE I

In the treatment of cancer of the breast in Stage I, we should recommend operation at once and at present we can properly limit the treatment to operation. Preoperative treatment will do no harm in these early cases, but it has not been proved of definite value. The primary treatment of this group by radium or radium combined with roentgen rays has not improved upon the results from operation, and I think has not equalled them. Some patients will absolutely refuse operation, and many postpone consulting a physician, thus delaying the treatment, because of the fear of an operation. Therefore, it is a matter of wisdom and good policy for surgeons not to tell the public that surgery is the only possible treatment. Some patients have been cured by irradiation alone. If this fact is made known, the patient may consult a physician early in the hope of avoiding an operation. He can then advise her properly.

We must always remember that it is possible that a very small tumor in the breast may be associated with distant metastasis at the time of the first examination or the original operation. Such metastasis accounts for the surgical failures in Stage I when the recurrence is not local. When such distant metastasis is found, the case must of course be classed in Stage III. In 29 per cent of the cases studied by Harrington, in which lymph nodes were not palpable in Stage I, metastases were found at operation. When axillary metastases are found at operation, the case must be classified in Stage II, and postoperative irradiation should be given, even if no preoperative irradiation has been used. Unfortunately, probably less than 10 per cent of *all breast cancers* come to the surgeon in this early stage (I), and only 20 per cent of the *operable* cases (Harrington) are still in Stage I.

RECOMMENDATIONS, STAGE II

Cancer of the breast in Stage II should be treated by preoperative irradiation, surgery, and postoperative irradiation. However, no combination of treatment can compensate fully for delay in diagnosis or operation, while the disease is still in Stage I. Of 2,396 operable cases (Stages I and II) coming to the Mayo Clinic (Harrington), 80.6 per cent were in Stage II. Judged by general surgical statistics from large clinics, as reported in the literature, only 23 per cent of this group can be expected to be alive after five years, but if irradiation is added to operation, nearly double the number should be alive after five years.

THEORETICAL AND BIOLOGICAL EVIDENCE FAVORING PREOPERATIVE IRRADIATION

(1) *The preoperative irradiation tends to devitalize or destroy the more malignant types of cells.* According to the microscopical

studies of carcinoma of the breast, four characteristic grades of malignancy have been recognized, and as a result the tumors have been divided into Grades 1, 2, 3, and 4 (Broders, MacCarty, Harrington, Ewing, Dawson and Tod). Of these Grade 1 represents the least malignant and Grade 4 the most malignant. Dawson and Tod state that these microscopical grades of malignancy can only be determined after complete operation and a study of the entire breast. While there is a general microscopical appearance in these tumors which permits classification and is helpful in determining the prognosis, as has been well shown by Harrington, some characteristics of all these grades are apt to be found in some part of each tumor. To make this point clear, I made inquiry of a number of our leading tumor pathologists, James Ewing, W. C. MacCarty, Stanley Reimann and Eugene Case. MacCarty writes: "In answer to your questions relative to different grades in different portions of a tumor: (1) Different portions and even different areas in the same microscopic field show different grades. (2) The grades of the primary and secondary tumors vary. (3) Recurrent tumors are often different in grade from the primary tumor. (4) Grades differ considerably, depending on who does the grading. (5) Different grades have different criteria. Personally, I know that the grading of tumors has only probability value when used clinically." Ewing says, "One can sometimes find different grades of malignancy in different portions of cancers, but this is the exception and not the rule. Generally, the tumor is uniform, but the peripheral areas are better nourished and more alive, and these are the ones we must sterilize by radiation or remove by surgery." Case says, "One commonly finds undifferentiated cells in tumors of a less degree of malignancy if a sufficient study of the tumor is made. They may be few in number, but when present they certainly affect the grading of an otherwise slowly growing tumor." Reimann says, "I hold the opinion that various grades of malignancy can be found in at least half of the tumors encountered in a service such as we have at our hospital and probably in 75 per cent if sufficient number of sections are taken from different areas."

In his studies of 2,396 operable cases (clinical operable Stages 1 and II), Harrington has shown that the microscopical grade of malignancy has much to do with the prognosis following operation for carcinoma of the breast. In his study, he found as high as 100 per cent five-year survivals in microscopical Grade 1, and as low as 17 per cent in Grade 4. It so happens that the microscopical Grades 1 and 2 which are more responsive to operation are the more resistant to irradiation, and Grades 3 and 4 which make up the great bulk of surgical failures are the more responsive to irradiation. It is quite logical, therefore, that the combination of irradiation and operation should give better results than either measure used alone, because most if not all tumors contain some of the different grades of malignant characteristics. It is true that Harrington's statistics do not indicate the expected great improvement in the results from combined treatment as compared with operation alone, and as is shown by other statistics, but it must be remembered that the surgery in his cases was done in one of the best surgical clinics in the world, but no preoperative irradiation is recorded and the postoperative irradiation, for the most part, was given at scattered points throughout the country. Our postoperative irradiation failures usually result from distant metastases in parts of the body where we have not irradiated. Therefore, the earlier the irradiation can be applied, before the disease has spread beyond the field of irradiation, the better will be the results.

Therefore, our greatest concern, both from the surgical and radiation standpoint, is connected with the microscopical Grades 3 and 4 in the clinical Stage II. These represent 91.4 per cent of the 1,907 operable cases in which there was glandular involvement (Harrington), and of these two more

malignant grades, only 20.5 per cent of the 481 traced patients, who had operation only, were living five years after operation. It must be clear, therefore, that our greatest problem is in dealing with the microscopical Grades 3 and 4, in the clinical Stage II. This group represents approximately 80 per cent of all operable cases. Even the cases classified as Grades 1 and 2 are likely to contain some of the more malignant cells; therefore when axillary nodes are present, all cases should have added to surgery both preoperative and postoperative irradiation.

It so happens that so far as the microscopical disease is concerned, Grades 3 and 4 are the most radiosensitive, while Grades 1 and 2 are the least radiosensitive. This, too, is a matter of common knowledge, and common agreement. Unfortunately, these same Grades 3 and 4 represent the type of disease which leads to early and extensive metastases. This is also shown by Harrington's studies in which 90 per cent of operable cases with lymph node involvement belong to Grades 3 and 4. It is also self-evident that unless the irradiation is applied while the disease is still in the area usually treated, ultimate failure will result. Again I must say, "The earlier the patients are irradiated, the better will be the results."

Probably no one has studied the pathology and the clinical behavior of carcinoma of the breast more than the late surgeon, Joseph C. Bloodgood. He said in 1935, "There is no danger whatever in giving pre-operative irradiation to clinical operable breast cancers. There is no danger in delaying the complete operation from two to three months if devoted to a thorough course of irradiation. I have some cases now in which, although the cancer cell is still to be stained in the microscopic sections, there is no growth, and in most of these early cases there is no evidence of metastasis. There was no growth in the tissue culture. There is an increasing number of operators, radiotherapeutists and pathologists who are beginning to feel that the moment pre-operative irradiation begins the danger of delay is averted, that is, that there is ample time to give as much irradiation as may be necessary.

"If there is no internal metastasis there is no danger of its taking place or of further involvement of the axillary glands after properly performed pre-operative irradation."

Based upon the fact that the more malignant type of cells (Grades 3 and 4) are rendered less malignant by even a moderate amount of irradiation (much less than is needed for complete destruction), it is fair to assume that such irradiation given to a patient with carcinoma of the breast will partially devitalize the more malignant type of cells, which is the cause of extensions and of the surgeons' failures. This should decrease the recurrences due to implantation during operation and should render less likely the dangerous lodgment of emboli which have been carried through either the lymph stream or blood stream, as a result of the manipulations concerned with the operative procedures. Such devitalizing effect upon the more malignant cancer cells surely occurs immediately after the treatment, even though it cannot be demonstrated microscopically. Therefore, there is no advantage from this standpoint in prolonging the interval before operation, and the operation can take place as soon as the proper amount of irradiation has been given into the tumor areas, which we are estimating to be about 900 r. I have seen tumor tissue reduced to half size within two weeks. Webster observed a case with multiple recurrent skin nodules. He treated one nodule and protected the others, for control. He found almost complete regression of the treated nodule in two weeks' time following 660 r. This tumor belonged to microscopical Grade 4 and was a recent recurrence.

(2) *The preoperative irradiation renders the normal tissues less receptive to implantation.* Biological experiments (Murphy, and Russ and Scott) indicate that, in addition to the effect of the irradiation on the malig-

nant cells, there is an effect on normal tissue which is detrimental to implantation of carcinoma. Russ and Scott have utilized rats and have exposed to the irradiation two of the opposing quadrants of the outer two-thirds of a circle of skin in the flank protecting the central area of the circle, and the other two quadrants. They then implanted malignant disease (sarcoma and carcinoma) in the unexposed center. In all instances, the tumor tissue grew by preference into the unirradiated areas. This effect was evident even when as little as 50 or as much as 200 per cent of an erythema dose was used and was also effectual even when the irradiation was given three days preceding the inoculation, or three days after inoculation. This retardation of growth was observed (1) when the entire rat was irradiated by repeated small doses of roentgen rays, and then inoculated; (2) when the inoculated tumor was protected and the surrounding tissue exposed; (3) when the test tumor was compared with control inoculation into unexposed tissue in the same animal, or with different animals.

With these facts in mind, preoperative irradiation is definitely indicated, especially in carcinoma of the breast in clinical Stage II. This preoperative treatment which I recommend can usually be given in approximately two weeks, and the patient can be operated upon usually during the third week. There is, therefore, no great delay in the operation and such irradiation will not interfere with the technical procedures of the operation itself. Preoperative treatment has been recommended by me since 1915, but until recent years relatively few cases have been referred for such treatment, and not enough patients have been given this short type of preoperative treatment to make any statistical statement of great value. We have not found that this type of preoperative irradiation interferes with the healing of the wound. Concerning preoperative treatment, Berven says, "In all instances, we have found advanced cancer contract in size and become more movable, but we have never seen a tumor increase in size from the first day in which we began treatment." This observation has also been made by Jüngling. The preoperative treatment has been proved, therefore, a definite interference with cancerous growth lasting at least six or eight weeks.

In the past, "preoperative" treatment has included three types of cases: (1) those of clinical Stage II, described above; (2) those belonging to Steinthal Group IIc which are doubtfully operable but which are made more operable by preoperative treatment, and (3) those which are totally inoperable but which, by prolonged treatment and after an interval of two or more months, are sometimes made operable. For the sake of brevity, I will confine this discussion of preoperative and postoperative irradiation to the group of cases with axillary nodes but which are still clearly operable (Stage II).

THEORETICAL AND BIOLOGICAL CONSIDERATIONS FOR POSTOPERATIVE IRRADIATION

Local postoperative treatment is intended (1) to destroy any malignant cells that may have been transplanted during operation; (2) to destroy any microscopical remnant of cancerous tissue which the surgeon may have missed, and (3) to render the normal tissue more resistant to cancerous growth. Definite evidence of implantation is furnished by the observance of stitch hole recurrences. Other more frequent implantations probably occur under the skin flap. It is our impression that remnants of cancerous tissue are rendered more malignant and also more radiosensitive by the congestion following the traumatism of operation. It is generally admitted that local and regional recurrences are the result of incomplete operation, but since 38 per cent of the failures have local recurrences and 15 per cent axillary recurrences (Creyssel and Morel), it is seen that the regional recurrences indicate incomplete operation in 53 per cent of the failures. All

my recommendations are intended not to replace surgery but to lessen the failures connected with surgery, for in those clinics where the basic principles of radiotherapy have been followed most closely, and where the radiologists have mastered a good technique, postoperative irradiation has become a routine procedure in all cases in which the disease has spread beyond the mammary gland. Hintze states that 80 per cent of the cases of breast cancer in the University Surgical Clinic in Berlin receive postoperative treatment, and postoperative treatment is advised by him in all operated cases. It is the accepted procedure in most of the large clinics both in this country and abroad.

Time for Postoperative Irradiation. A review of my own records as well as a study of the literature shows that many patients are sent for "postoperative" treatment at a time when they actually have evidence of recurrent disease. It is my opinion that to obtain the most benefit from postoperative treatment, the patient should be referred as soon after the operation as the general condition and circumstances of the patient will permit, which is usually within ten days to two weeks, even though the wound is not entirely healed. This is especially important if no preoperative irradiation has been given. If preoperative treatment has been given, it may be well to wait three weeks after the end of the preoperative treatment. I have found, and in this Webster agrees, that early recurrences are more likely to be radiosensitive than the same recurrence after it has become firmly established in its location. Theoretically, one can assume that tissue of microscopic size is more easily destroyed than the same tumor after it has become macroscopic. This makes it important to give the irradiation as soon after the operation as is practical. We have not found that postoperative irradiation interferes with the healing of the wound, nor have we found that the wound breaks down because of postoperative irradiation, providing one does not exceed the "saturation dose."

Ovarian Sterilization as a Preoperative or a Postoperative Prophylactic Measure. It is well known that cancer of the breast is more malignant in young women (Sistrunk and MacCarty, Lee, Dresser). Lee says, "Of the patients 40 years or under, 27 per cent were alive and well at the end of five years, whereas, of those over 40 years of age, 45 per cent were alive and well at the end of five years." Dresser finds, "Of 48 women under 40, treated by radical mastectomy, only 12.5 per cent were free from disease at the end of three years." Cancer of the breast also grows more rapidly during pregnancy (Bagg, Steel). Trout collected 15 cases in which pregnancy occurred after operation and of these, 87 per cent developed carcinoma in the remaining breast. Therefore, pregnancy should be avoided when cancer of the breast is present. Experimental evidence indicates that the ovarian hormones stimulate the production of cancer of the breast in animals which have any susceptibility (Loeb, Lacassagne, Gardner). In recurrent or metastatic disease from cancer of the breast, oophorectomy (Schinzinger, Beatson, Lett, Boyd, Torek, Thomson, Paterson), and also ovarian sterilization by irradiation (Foveau de Courmelles, Dresser, Sittenfield, Hoffman, Ahlbom, Witherspoon, Wintz) has been followed in a considerable number of cases by a disappearance of the lesions. A woman who has had carcinoma of the breast is proved to be susceptible to the disease, and Harrington's statistics indicate that 75 per cent of the operable cases have remnants of the disease in the system after operation, or they would not have died of the disease within five years. Consequently any stimulation in such cases is likely to shorten life. Therefore, we recommend ovarian sterilization in all women who are still having menstruation. Reports by Torek and statistics by Ahlbom seem to indicate some value of ovarian treatment even after the menopause. Ahlbom says, "The mode of reasoning on which these experiments have been based has been that a certain internal se-

cretory function remains in the ovaries for some little time after the menopause." Dresser, on the other hand, has not been able to recognize any benefit after the menopause.

TECHNIQUE

The technique of radiation therapy in cancer of the breast has varied tremendously not only among different radiologists but even in our own experience. This is quite natural for radiotherapy has been a very rapidly developing procedure. There has accumulated new knowledge both concerning the disease and concerning the radiation effects since the discovery of the roentgen rays approximately forty-two years ago, and the therapeutic use of these rays has been particularly developed during the past thirty-eight years, beginning with a few scattered workers and gradually spreading until now it is not only universally utilized throughout the world, but is being used in all branches of medicine. My own experience in treating carcinoma of the breast covers a period of over thirty-six years, and naturally, there has been a considerable variation in technique during this evolution. No technique can be standardized even yet. Considering general principles, my own technique from the beginning to the present time has involved the use of fractional dosage carried over a considerable period of time. Therefore, instead of reviewing all that has been done and the variations that have taken place, I will be content with the description of my own technique which may be again modified as newer knowledge is developed.

Technique for Short Preoperative Treatment. This will apply to that group of cases which are still clearly in an operable stage but in which the disease is no longer confined to the mammary gland. The object in this group of cases is to devitalize the more malignant type of cells with moderate dosage without causing undue delay nor interference with the operation itself. Ordinarily, I aim to finish this preoperative treatment in approximately two weeks. If ovarian sterilization is given as part of the preoperative treatment, three weeks will be required. During this time, I aim to give approximately 900 r through each side of the breast and through the axillary and supraclavicular region. The cross-fire value of this will equal approximately 900 r in the diseased area. For all this treatment, I utilize 200 kv., 50 cm. distance and 0.5 mm. of copper filtration. For portals (Fig. 2) I

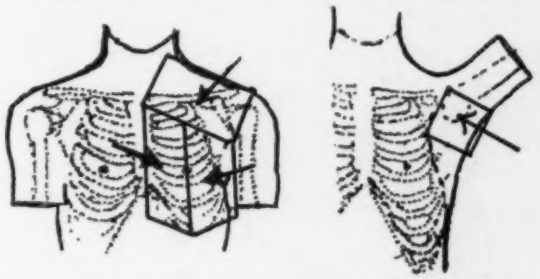

FIG. 2. A diagrammatic illustration of the outline of the portals for *preoperative* irradiation of the breast. See description in text.

utilize the space from the parasternal line to the nipple line, turning the patient on the side and irradiating tangentially (Holfelder) so that the rays will include the chest wall but not penetrate the lungs. A similar tangential dose is given through the mammary area externally, extending from the midaxillary line to the nipple line also tangentially, avoiding penetration of the lung but including the chest wall. An axillary portal occupies the space between the posterior and anterior axillary folds, and the rays are directed upward and inward so as to irradiate the axilla, the coracoid or intraclavicular region and the deeper portion of the supraclavicular area, again utilizing tangential rays and including the chest walls and the upper mediastinum. A portal is then utilized including the supraclavicular region and the coracoid region, including an area from the lower border of the axillary fold upward and inward to the sternoclavicular junction, and in stouter persons, a similar portal is utilized through the posterior axillary field, carrying out the same general principles. This should distribute the radiation rather evenly and should give approximately an erythema dose to all of these tissues. This amount of

radiation is intended to be supplemented by postoperative irradiation.

The preoperative technique described by Adair differs from the above, and was used with a different object in view. He studied 117 operable cases of breast cancer, each having a preliminary biopsy positive for cancer. Observations were made both clinically and microscopically to note the

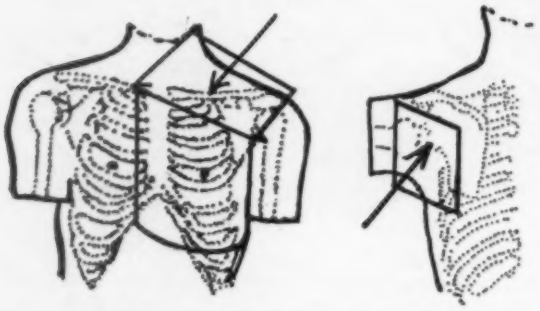

Fig. 3. A diagrammatic illustration of the portals commonly used for *postoperative* irradiation of the breast. See description in text.

effect of preoperative irradiation. Sixty-five cases were treated by the 200 kv. roentgen machine, and 52 cases by the 4-gram radium element pack. The roentgen rays were given through five different portals, and varied in dosage from 1,200 r per portal (36 cases); 1,500 r per portal (11 cases), and 1,800 r per portal (18 cases). His object was to determine just how much total effect could be shown at the subsequent operation; his study does not involve five-year end-results, therefore it is discussed separately. He found that 1,800 r per portal gave the best results—33 per cent complete disappearance of the breast cancer, and 22 per cent complete disappearance of the axillary nodes. The radium packs gave 35 per cent, and 13 per cent respectively. The time of the operation after finishing the preoperative irradiation varied from twelve days to three hundred days, and the average sixty-six days. The majority of cases were operated upon two months after finishing the preoperative irradiation. It is clearly seen that the object as well as the technique of this form of preoperative irradiation differs from that which I have recommended above. Adair says, "In all instances, irradiation caused clinical reduction in the volume of the breast tumor. To a lesser extent this was true of the axillary disease. The tumor tissue softens and commonly takes on the same consistence as the mammary tissue."

Technique of Postoperative Irradiation. I have been confining my postoperative irradiation to the side of the chest from which the tumor has been removed, including the axilla, supraclavicular region and mediastinum. It is impractical to treat the entire body. Creyssel and Morel have found 73 per cent of recurrence and metastases in this region (scar and skin 38 per cent; axillary 15 per cent; supraclavicular and carotid region 20 per cent; bone 20 per cent; pleuropulmonary 19 per cent; liver 2.4 per cent; other breast 2.4 per cent; other axilla 2.4 per cent; peritoneum 1.6 per cent). I usually begin postoperative treatment through a portal (Fig. 3) occupying the supraclavicular and coracoid region, outlined approximately similar to the one utilized in the preoperative treatment, and for a second portal of entry, I usually use the posterior axilla, with the arm thrown over to the opposite shoulder and the rays directed into the axilla, into the deeper part of the supraclavicular region and toward the upper mediastinum. Generally the arm cannot be abducted sufficiently to get a portal of entry into the axilla itself after operation. As a third field, I utilize a large area extending from the lower border of the coracoid and supraclavicular portal to the level of the epigastrium and extending from the right border of the sternum to the left anterior axillary fold. Because of this large area involved, because of the lung and heart underneath and because of the fact that this area is very apt to give rise to radiation sickness, I give relatively smaller doses over this field. I utilize for postoperative treatment over this portal the so-called low voltage technique, using 135 kv., 2 mm. aluminum filtration and 50 cm. distance. Generally, I can only give about 200 to 300 r in each application, sometimes

less, but I aim to deliver into this area a total of approximately 1,800 to 2,400 r, counting both preoperative and postoperative treatment. The treatment is given according to the "saturation technique," and we should not exceed a full erythema used, while the congestion is present and while any cells that have been implanted or transferred are not yet completely adapted to the tissues of the host, and while the cancer cell is more radiosensitive than it would be at a later date.

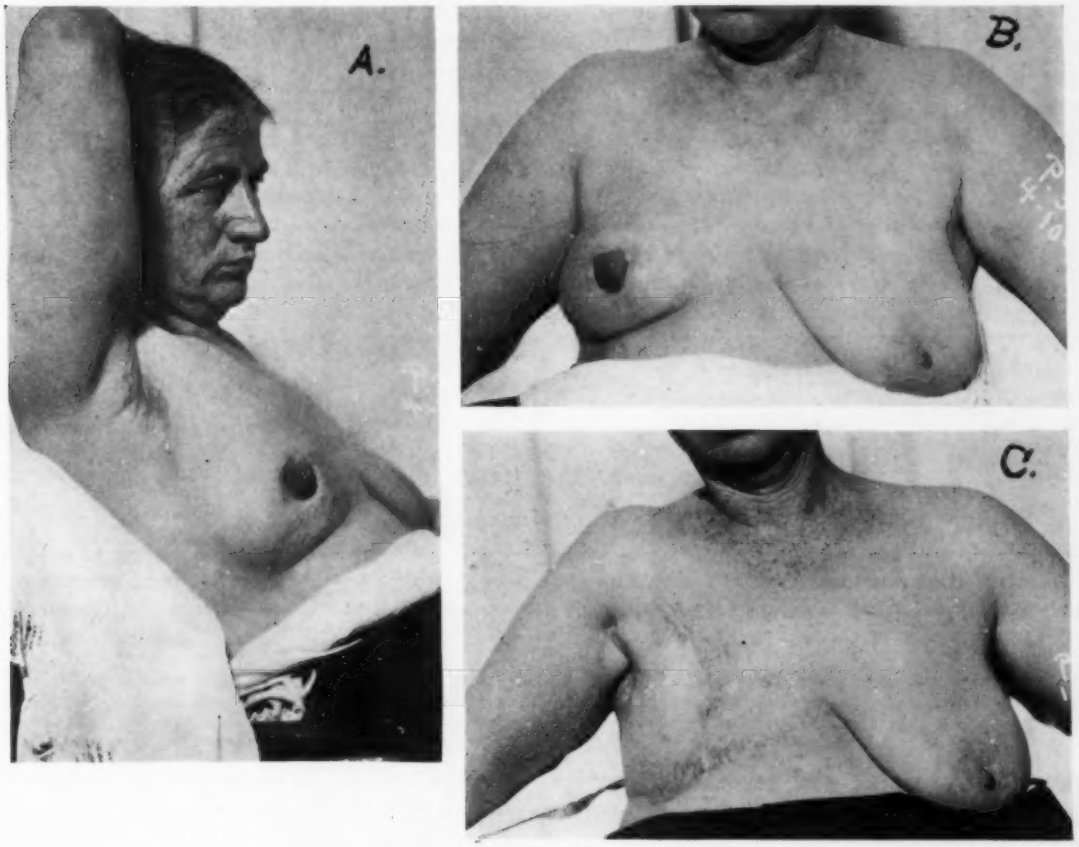

Fig. 4. This illustrates carcinoma of the breast in clinical Stage III, which is totally inoperable at the beginning, but which can be made operable at times by preoperative irradiation. This patient was a woman, aged forty-eight, who was referred to me on April 10, 1923, by Dr. F. A. Mantz of Philadelphia, for preoperative treatment. After preliminary irradiation, she had a simple amputation of the right breast by Dr. Mantz, July 6, 1923. She remained free from any evidence of carcinoma, and died of apoplexy May 14, 1930, or approximately seven years after beginning the preoperative roentgen treatment.

dose at any time. The aim is to deliver into the axilla, coracoid and supraclavicular region approximately 1,800 to 2,400 r. This will bring about a definite erythema but I have not found that it interferes with the healing of the wound nor the convalescence of the patient. I believe that treatment should begin about two weeks after operation if no preoperative irradiation has been

Recommendations, Stage III

This group includes all cases with adherent or edematous breasts or adherent axillary nodes with supraclavicular or visceral involvement, or distant metastases (Fig. 4). The discussion of the treatment of cancer of the breast in clinical Stage III must be brief, and yet this group demands more detailed consideration than the others. These

cases should be considered primarily inoperable. Portmann has shown that the lives of this group are shortened by primary operation. This group should be treated primarily by irradiation. Then, after a period of two or more months, the remaining disease should be removed if practicable. It is this group of borderline cases for the most part that have been classed in statistics as having had preoperative treatment, and, as a result, one should not expect results equal to those operated upon in an early stage. In this group, especially, every case must be individualized. During about twenty years, it has been my practice with every case of cancer of the breast to make roentgenograms of the chest, spine (anteroposterior and lateral) and the pelvis. During recent years, I also examine the skull. At times, I find unsuspected metastases, but whether any metastasis is found or not, such films always serve as a record for comparison when subsequent symptoms of metastasis arise.

In a considerable number of these cases, one succeeds in controlling the disease in the area treated by irradiation, and then we still fail on account of distant metastases. These more advanced cancers of the breast are best treated by fractional doses given according to the "saturation method," continued over a period of from four to six weeks or longer, but at no time should one exceed the normal tissue tolerance. By cross-fire method, irradiation should be given as uniformly as possible throughout the tumor tissue including the regional lymphatics; the tangential method as advised by Holfelder should be used. In this group of cases, 200 kv., 0.5 mm. copper filtration, at 50 cm. distance will be most practical. At times, 2 mm. copper filtration will be found very useful. Risk is involved of normal tissue degeneration when one exceeds a total of more than 4 to 6 erythema doses (4,000 r) over any one area of skin or subcutaneous tissue, even if only a moderate erythema has been present at any one time. After a period of two or more months, when the tumor tissue has shown definite contraction, and has become more movable, and when the axillary lymph nodes have contracted or have disappeared, I believe it is advisable to remove the breast and any palpable nodes.

TABLE I

RECENT COMPARATIVE STATISTICS FROM THE SAME CLINICS

Surgery Alone Percentage Living 5 Years				Surgery and Irradiation Percentage Living 5 Years			
Author	No. Cases	Stage II	All Operated Cases	Author	No. Cases	Stage II	All Operated Cases
Siemens	104	33.6		Siemens	188	53.2	
Harrington*	604	24.3		Harrington	1447	28.8	
Gentil and Guedes	42	20.6		Gentil and Guedes	83	42.5	
Adair		20.0	35.0	Adair		23.0	40.6
Hintze	656		30.5	Hintze	183		53.0
Portmann	85		35.6	Portmann	99		46.0
Ganz (Schinz)	3599		31.2	Ganz (Schinz)	118		40.0

Remarks: It can be seen that the end-results have been improved by postoperative irradiation as compared with operation alone from 11.4 per cent to 73.7 per cent in all cases, and when applied to Stage II, from 15 to 110 per cent, according to different authors.

* The surgery in this group of cases, reported by Harrington, was done in the Mayo Clinic, but the postoperative irradiation was given mostly by radiologists scattered throughout the country. It is self-evident that, under such circumstances, the irradiation is not likely to be on such a relatively high plane as the surgery.

RECURRENT CARCINOMA OF THE BREAST

Recurrent carcinoma of the breast is nearly always a difficult irradiation problem. If the disease is localized, one can use

TABLE II

RECENT COMPARATIVE STATISTICS FROM VARIOUS CLINICS AS COLLECTED FROM THE LITERATURE

Surgery Alone Percentage Living 5 Years				Surgery and Irradiation Percentage Living 5 Years			
Author	No. Cases	Stage II	All Operated Cases	Author	No Cases	Stage II	All Operated Cases
Lane-Claypon	2,000	24.7					
Hutchison		25.0	28.1	Hutchison		41.0	40.9
Dawson and Tod	5,615		34.3	Dawson and Tod	1785		44.4
Hintze	4,952		28.4	Hintze	2822		37.9

Remarks: This group of statistics represents cross-section statistics collected by various authors from large clinics in various parts of the world. Even this collection shows a gain of approximately 25 per cent in the results of postoperative irradiation added to operation as compared with surgery alone.

TABLE III

RECENT COMPARATIVE STATISTICS OF RESULTS AS COLLECTED FROM SPECIAL CLINICS

Surgery Alone Percentage Living 5 Years				Surgery and Postoperative Irradiation Percentage Living 5 Years			
Author	No. Cases	Stage II	All Operated Cases	Author	No. Cases	Stage II	All Operated Cases
Harrington	1911	25.0	33.1	Westermark	70	38.0	37.0
Gould	151	22.0	33.1	Evans and Leucutia	175	46.3	46.1
Abell	217	26.0	46.0	Wintz	97	51.5	
Redman	106	41.0	44.0	Lee	217	53.0	41.0
Jessop	216	30.5	48.0	Weisswange	171	27.1	53.7
Klingenstein		17.0	23.0	Billich	164		39.6
Lewis and Rienhoff	420		18.0	Gäbel and Magens		33.3	47.7
Gask			36.0	Holfelder	118		50.0
				Webster	358		42.0
				Nicolson and Berman	74		36.8
				Hummel	115		68.7
				Pfahler and Vastine	269	52.0	52.4
Average percentage		27.9	35.0	Average percentage		39.6	46.8
				Preoperative Irradiation, Surgery, and Postoperative Irradiation			
				Trout			55.0
				Westermark	44	46.6	52.0
				Wintz	97		51.0
				Pfahler and Vastine	91	57.1	47.2
				Average percentage		51.8	51.3

Remarks: (1) It will be observed that in these special clinics where special attention is given to the results, they are better by operation alone, and also by operation combined with irradiation. There is an average gain of 42 per cent in Stage II and of 40 per cent when all operable cases are counted, but the best records show that a 50 per cent five-year recovery is possible.

(2) It should also be noted that the records for *both* preoperative and postoperative irradiation give better results than the mere addition of postoperative irradiation.

(3) The average of the percentages obtained by these authors shows a definite advantage for both postoperative irradiation and for the combination of preoperative irradiation, surgery and postoperative irradiation.

TABLE IIIA

FIVE-YEAR RESULTS, RELATIONSHIP BETWEEN INVOLVEMENT OF AXILLARY NODES AND GRADE OF MALIGNANCY (HARRINGTON, 1935)

Treatment	Grade of Malignancy	With Involvement of Axillary Nodes—Stage II			
		Patients Operated Upon		Lived 5 or More Years after Operation	
		Total	Traced No.	Patients	Traced Per Cent
44 Cases = 9%	1	4	4	4	100.0
SURGERY ONLY	2	40	38	22	57.9
500 Cases = 91%	3	174	165	45	27.3
	4	326	316	54	17.1
129 Cases = 10%	1	8	8	8	100.0
SURGERY + X-RAYS	2	121	107	49	45.8
1,234 Cases = 90%	3	456	424	135	31.8
	4	778	732	160	21.9

Remarks: The *surgery* in the above group was done in one of the greatest clinics in the world. The *postoperative irradiation* was done at scattered points throughout the country. These statistics involve 2,396 operated cases; 1,907 of these, or 79.6 per cent, had lymphatic involvement, and 489, or 20.4 per cent, of the 2,396 operated cases had no axillary nodes.

TABLE IV

CASES ALIVE FIVE YEARS HAVING HAD PREOPERATIVE IRRADIATION, SURGERY AND POSTOPERATIVE IRRADIATION (PFAHLER)

Stage I	Stage II	Stage III
Surgery within 30 Days after Beginning Preoperative Irradiation and Followed by Postoperative Irradiation		
9 of 11 = 81.8%	13 of 23 = 56.5%[a]	0 of 7 = 0
This Same Form of Treatment Less Than 5 Years Ago		
4 of 4 = 100%	7 of 10 = 70%[b]	0 of 2 = 0
Operated from 30 to 60 Days after Beginning Preoperative Irradiation Followed by Postoperative Irradiation		
2 of 4 = 50%	5 of 7 = 71.4%	0 of 3 = 0
Preoperative Irradiation and Operated More Than 60 Days after Beginning Preoperative Irradiation		
8 of 11 = 72.7%[c]	6 of 12 = 50%[d]	0 of 13 = 0[e]
Total Traced Cases in Stages I and II Living Five Years after Preoperative and Postoperative Irradiation		
19 of 26 = 73%	24 of 42 = 57%	0 of 23 = 0

[a] One additional case not traced.
[b] Two additional cases died of intercurrent disease and not included.
[c] One died of intercurrent disease.
[d] One died of intercurrent disease—two not traced.
[e] Three died of intercurrent disease—one not traced.

intensive local treatment, preferably with radium, but quite successfully with roentgen rays. If the recurrence is widespread, or there are extensions into the subcutaneous and cutaneous tissue (erysipelas carcinomatosum) one may control the disease for a time, even a year or two, but ultimate failure is the rule. We have treated 491 cases of postoperative recurrences following breast surgery. Of those in which there was local recurrence, 39.7 per cent were well five years. Of the cases in which there was axillary or supraclavicular recurrence, 23.3 per cent were well five years, and 18.5 per cent of all the recurrent and metastatic cases, regardless of location, were alive and symptom-free five years after first coming under my care. Distant metastasis in the lungs or bones usually means that the disease has spread by emboli through the blood stream and a general carcinomatosis is likely to develop sooner or later. In such cases, one can more or less control individual lesions or areas of disease, but other areas become involved and ultimate failure is the result. I have seen cases with metastatic carcinoma of the lung disappear, and the patient live four years, and I

TABLE V

PATIENTS ALIVE 5 YEARS AFTER HAVING HAD SURGERY AND POSTOPERATIVE IRRADIATION (PFAHLER)*

Treated between 1902 and 1922

	Without Glands	With Glands
	At time of operation	
Alive and well	35 = 66.0%	46 = 40.7%
Dead of carcinoma	18	67
Dead of intercurrent disease	3	5
Not traced	6	13
Total	62	131

Treated between 1922 and 1932

	Stage I	Stage II	Stage III	All Operated Cases
Alive and well	32 = 72.7%	26 = 52.0%	2 = 22.2%	60 = 58.2%
Dead of carcinoma	12	24	7	43
Dead of intercurrent disease	4	5	0	9
Not traced	1	2	2	5
Total	49	57	11	117

Even if all cases not traced or dead from intercurrent disease are counted as failures, there still remains 51.3 per cent living five years after treatment.

All Cases Treated Prior to 5 Years ago by Surgery and Postoperative Irradiation

Alive and well	141 = 52.4%
Dead of carcinoma	128
Dead of intercurrent disease	17
Not traced	24
Total cases	310

If all dead and untraced patients are counted as failures, there still remains 45.5 per cent success.

All Cases Treated Prior to 5 Years ago by Surgery and Preoperative or Postoperative Irradiation or Both

Alive and well	181 = 51.1%
Dead of carcinoma	176
Dead of intercurrent disease	24
Not traced	28
Total cases	412

Counting all dead and untraced patients as failures, there remains 44.6 per cent success.

* From Dr. Pfahler's private records.

233 cases of primary carcinoma of the breast treated by irradiation only, not included in the present analysis.

491 cases of recurrent carcinoma of the breast following operations, treated more than two months after operation and cases in which there was definite recurrence when first seen by us, are not included in the above analysis.

The "five-year" record in our cases begin with the dates of beginning our treatment.

have seen metastatic carcinoma of the bone heal and the patient live five years. Perhaps with the associated ovarian sterilization, these results may possibly be improved or made permanent.

RESULTS OF TREATMENT

Working at the University of Frankfurt, Holfelder finds that thorough scientific postoperative irradiation gives an average of double the number of cases which are

symptom-free after five years as compared with operation alone. It is difficult to estimate the results of treatment, because of the difficulties in classification. The technique has been variable, therefore my conclusion must of necessity be open to criticism and skepticism. Portmann has tried to solve this problem by a careful analysis of cases taken from the records of the Cleveland Clinic, and has proved with his critical analysis that postoperative irradiation is of value, but until some large institution with a large amount of material can have a large group of cases carefully studied and classified before operation, operated upon by a standard technique or, at least, by equally skillful surgeons, and then treated by equally skillful radiologists with a more or less standard technique, and then wait until five or ten years after such a group has been studied, it will be difficult to draw conclusions that are not open to criticisms. Such criticisms, however, apply to most clinical work. It is often forgotten that an equal or greater amount of variation in skill and technique is found among radiologists than is found among surgeons. After all, the apparatus used by the radiologists corresponds very closely to the surgical instruments used by the surgeon, and more depends upon his skill and judgment than upon the particular instruments that are used.

TABLE VI

RESULTS OF TREATMENT OF POSTOPERATIVE RECURRENT CARCINOMA OF THE BREAST (491 CASES FROM DR. PFAHLER'S PRIVATE RECORDS, REVIEWED BY DR. VASTINE)*

Symptom-free Five or More Years after Beginning Roentgen Treatment	Per cent
Local recurrences	39.7
Axillary or supraclavicular recurrences	23.3
Cases with distant metastases	5.1
Total recurrences and metastases regardless of location	18.5

* This group of cases admits of no doubt as to diagnosis. This disease may lie dormant eighteen to twenty years. Therefore, we cannot say that they are well.

I am submitting, therefore, a few tables bearing upon this subject, made up from a relatively few of the many statistics available in the literature. Time and space will not permit of a review or mention of all valuable contributions. Those compiled from recent literature and those made up from my own records must be accepted for what they are worth, but, at least, I as a clinical observer am thoroughly convinced of the value of both preoperative and postoperative irradiation in Stage II. I am indebted to my associate, Jacob H. Vastine, for a review of the cases from my private records.

SUMMARY AND CONCLUSIONS

(1) The treatment of carcinoma of the breast should vary with the clinical "stages" of the disease, and with the microscopical "grades" of malignancy.

(2) In Stage I, 70 per cent should be cured by operation alone, but only 10 per cent of all cases reach the surgeon in this early stage. Education of the laity and alertness of the profession should increase this number.

(3) In Stage II, only about 23 per cent are cured by operation alone. This number should be doubled by adding skillful preoperative and postoperative irradiation.

(4) The cases in Stages III and IV should be treated primarily by irradiation supplemented by surgery when practicable.

(5) Advanced carcinoma of the breast (Stages III and IV) should be treated primarily by irradiation and perhaps by surgery later. The disease can be retarded, the patient made more comfortable and perhaps cured.

(6) Recurrent carcinoma is usually best treated by irradiation. If the lesion is local and movable, excision by the knife or electrothermic needle may be better.

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THE ROENTGENOLOGICAL RECOGNITION OF CERTAIN BRONCHOMYCOSES INVOLVING OCCUPATIONAL RISKS*

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RECOGNITION of fungous disease in man dates from the discovery of the *Oidium albicans* of thrush by Langenbeck in 1839, but the science of mycology goes back to 1677 when Hooke discovered that the yellow spots on the leaves of roses consisted of filamentous fungi. Microfungi exist as parasites or saprophytes, or both, on almost every growing and decaying thing, but the majority are non-pathogenic to man. Most of those which cause human disease are found in the large class of fungi imperfecti or Hyphomycetes. They can be grouped into:

(1) The yeast-like fungi, which include *Monilia*, *Cryptococcus*, *Saccharomyces*, *Blastomycoides* and *Endomyces*.

(2) The filamentous fungi: (*a*) of the slender type, viz., *Nocardia*, *Anaeromyces* and *Vibriothrix;* (*b*) of the larger type, viz., *Oidium* and *Hemispora;* (*c*) with characteristic fructifications, viz., *Aspergillus*, *Penicillium*, *Mucor*, *Rhizomucor*, *Acremoniella*, *Sporotrichum*, *Acladium*, etc.

The spores of many of these fungi have a diameter of only 3–5μ, and can therefore easily enter the smaller bronchi and alveoli, and many are readily dust-borne.

The infection of lung tissue by microfungi (the so-called bronchomycosis or pneumomycosis) has been recognized and received considerable attention in the United States of America and also on the Continent for many years. Valuable work has recently been published by Dodge,[13] Jacobson,[15] and Carter.[5] In Great Britain, however, the bronchomycoses are either less frequent than in other countries, unrecognized or unrecorded. We have become more fungus minded in the last year or two, so much so that in some of the chest hospitals when tubercle bacilli are not found in the sputum of patients, fungi are suspected and sought for as a routine. Work in this field has been done by Castellani,[8] Castellani and Chalmers,[9] Ramsbottom[26] and others, and in Jersey (Channel Islands) by Marett[20,21,22] and his coworkers, Oliver[23,24] and Wood.

In my remote corner of England, practitioners are now realizing the importance of fungi, and it is surprising how often bronchomycosis can be found when it is systematically sought. I believe that, unknowingly, I treated many such cases when in general practice, numbers of striking cases of obstinate asthma, bronchitis and bronchopneumonia which ultimately recovered, on a mixture of potassium iodide and creosote, drugs urged by my father, as the result of many years of experience. We had no thought of fungi in those days, and did not recognize that we were employing powerful fungicides. It never occurred to us that we might be dealing with mycotic disease, yet the farmers themselves had long recognized the pulmonary irritation resulting from work with *mouldy* hay, and spoke of being "mou'ded."

In recent years I have been particularly interested in the roentgenological appearances found in the chests of agricultural workers following the inhalation of the mouldy dust of hay or grain. To this I have given the name of bronchomycosis feniseciorum (of haymakers or harvesters (Fawcitt)).[14] A similar condition has also been described by Campbell.[4] The incidence is seasonal and definitely depends upon a mouldy condition of hay or grain after a wet season. In the spring, when the hay is old and dusty, a dense white cloud arises when it is being fed to the stock or

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

when the barn is being swept. Sometimes the disease is associated with grain, and usually coincides with threshing time. The condition may appear as an epidemic. Practically all the patients are found among agricultural laborers and stable workers. The outstanding symptom is dyspnea. It is so marked that no other symptom seems of any importance.

The first diagnosis is almost invariably tuberculosis, but when repeated sputum examination is negative for tubercle bacilli, yet constantly shows the presence of microfungi, one cannot help suspecting these as the causal agent. In a series of some 25 cases of mycotic infection of the lung referred to me for roentgen examination during the last three years, all the patients were suspected cases of tuberculosis. Some, in fact, had been patients in sanatoria. In contrast to the cases described by Carter[6] no bone infection occurred in my series.

I am not blind to the fact that microfungi are ubiquitous and contaminants a constant danger, and accordingly special care is taken in the collection of specimens of sputum as described in a previous paper.[14] The establishment of their pathogenicity is extremely difficult to prove, but the clinical picture and the response to treatment are very striking in these cases, and I believe that, under certain conditions (I am of the opinion that certain microfungi have periods when they are pathogenic and periods when they are not), fungi can give rise not only to symptoms, but also to lung changes showing a characteristic roentgen picture due to mycotic infection of the lung. Roentgenologists should look out for the type of case in which, in the absence of tuberculosis, they should ask for an investigation of the sputum for microfungi. Prompt diagnosis is important because, in its early stages, the condition is curable by potassium iodide therapy and autogenous vaccine, but may become incurable later, progressing to the dense fibrotic, or stage of calcareous nodulation, as described by Virchow[31] (1856), Sutherland,[29] Sayers and Meriwether,[27] and others; or it may provide a soil for the growth of more serious disease by interfering with ciliary action and allowing such slow-growing organisms as the tubercle bacillus, or malignant disease, or get a foothold.

The symptoms and history vary according to the causative fungus. There are several types.

TYPE I. THE MYCOSIS OF HAYWORKERS

Workers with mouldy hay may get a mixed infection of *Aspergillus*, *Penicillium* and *Mucor*, the fungi of rotting vegetable matter. They suffer from gradually increasing dyspnea which goes on for a month or more until finally it is very acute and they cannot walk up the slightest incline. During this period any further contact with mouldy hay may produce exacerbation of the symptoms. They cough, and sometimes bring up scanty, frothy sputum. They show a slight fever and accelerated pulse rate. Examination of the blood was carried out in a series of 5 cases of Campbell,[4] but beyond a slight increase in the sedimentation rate there were no changes of any moment except a slight degree of leukocytosis. Rise in blood pressure was not observed. The sputum contains fungi but no tubercle bacilli. The clinical signs are those of a fine bronchial catarrh or asthma. Patches of dulness and crepitations, râles, rhonchi, and increased vocal resonance may be found. In more severe cases shortness of breath is extreme, and there may also be mucopurulent sputum, hemoptysis, emaciation, slight fever and myoidema. Sometimes the sputum smells like brewers' yeast. Except in chronic cases the chest expansion is normal.

Appearance in the Roentgenogram

Early stage. Roentgen indications are scanty but important. The lung markings are more defined than normal, in that the fine reticulation and shadows of peribronchial vessels are more evident, resembling a lymphangitis. Certain types and mild cases may not progress beyond this stage.

Second stage. This often follows very rapidly on the first and is characterized by rather soft snowflake mottling, widely distributed throughout both lungs; it lacks the peripheral distribution and the sharp definition and density of the typical silicotic nodule, and resembles the indefinite changes of bronchitis rather than a miliary tuberculosis. There is a tendency for the midlung fields and bases to be affected more than the apices. Emphysema is common, mainly seen at the bases, and, because of this, mycosis may be confused with pneumoconiosis, but the sudden onset and clinical history differentiate it. In miliary tuberculosis the nodular appearance is more discrete and evenly distributed throughout the lungs—i.e. the apices are equally affected—and emphysema is not present. These appearances are frequently seen in the lungs of hematite iron-ore miners, and even in surface workers. This is the stage at which most of my patients have been first examined; it is the acute stage, and may be misinterpreted in the roentgenogram.

Third stage. The progress to the third stage is gradual; in an advanced second stage there is a definite increase in the hilar and perihilar shadows, and glands may become evident. There is a gradual increase in the density of the mottling, particularly towards the bases, and a tendency to an elongation and narrowing of the heart shadow, and some limitation in the excursion of the diaphragm. The condition is now becoming chronic, *or healing*. Healed cases all show increased linear markings.

Fourth stage. The third stage gradually merges into the fourth, when the lungs may show patches of density due to coalescent areas of fibrosis, much more marked restriction of the diaphragm movements and a recurrence of emphysematous areas; and the linear markings are *much* exaggerated. This stage frequently reveals a widening of the previously narrow heart shadow, heralding cardiac embarrassment and disability. As the condition progresses, fibrous rings may appear, walling off small cavities

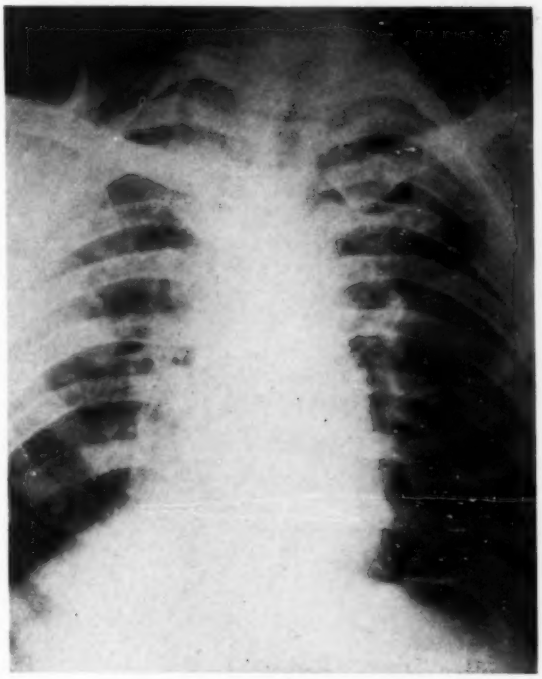

Fig. 1

or surrounding calcified nodules. In another variety the infection produces bronchiectasis. I have recently seen a case of superadded tuberculosis. Such cases have been described by Bethune and Moffatt,[2] Castellani,[8] Lapenta,[18] Wheaton,[32] and others. Kampmeier and Black[16] describe the condition associated with bronchial carcinoma.

There is an old saying, "One picture is worth a thousand words," and the roentgenograms will demonstrate the types of cases better than I can describe them.

Figure 1 is a roentgenogram of the lungs of a man, aged thirty-nine, who had suffered for two years from gradually increasing dyspnea, which he attributed to the effects of a smoke-like dust rising from hay in which he worked. The chest was hyperresonant and on deep breathing showed moist sucking sounds; repeated sputum examination failed to reveal tubercle bacilli, but a diagnosis was made of "galloping consumption" owing to the rapid deterioration. The illness ran an intermittent and protracted course. He had no fever, cough, or sputum, except in the morning or on exertion. The roentgenogram shows a somewhat barrel-shaped chest with marked limitation of

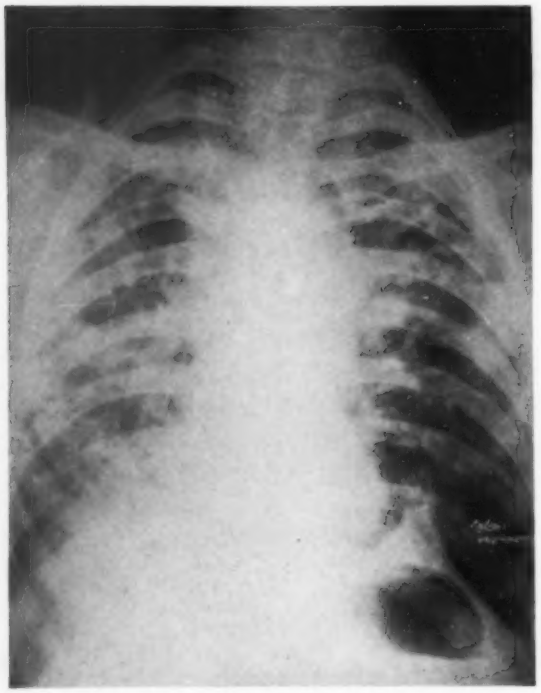

FIG. 2

the diaphragm movements, and extensive mottling and fibrosis throughout both lungs. The heart was pulled over to the right, and there was marked tachycardia. The honeycomb

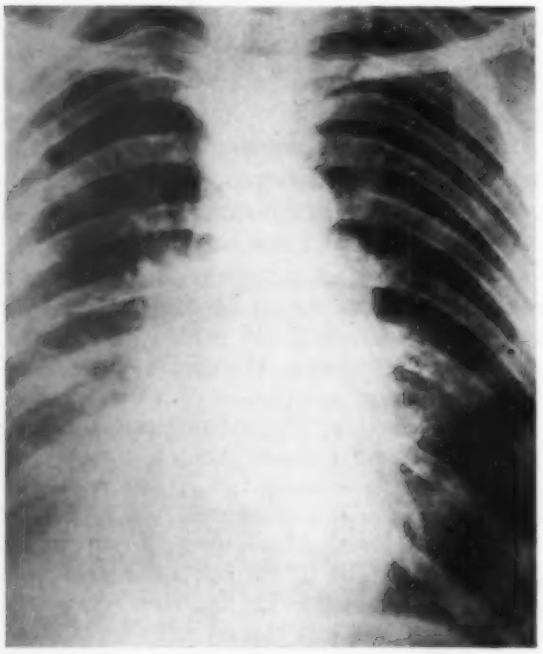

FIG. 3

appearance below the right clavicle suggests fibrous rings around the alveoli, in addition to thickened peribronchial vessels. Faulds, the Cumberland County pathologist, found aspergilli in the sputum, and the patient was put on intensive potassium iodide therapy, with little benefit. Six months later Professor Ramsbottom, the Keeper of Botany of the Natural History Branch of the British Museum in London, found species of *Aspergillus*, *Penicillium* and *Mucor* in his sputum.

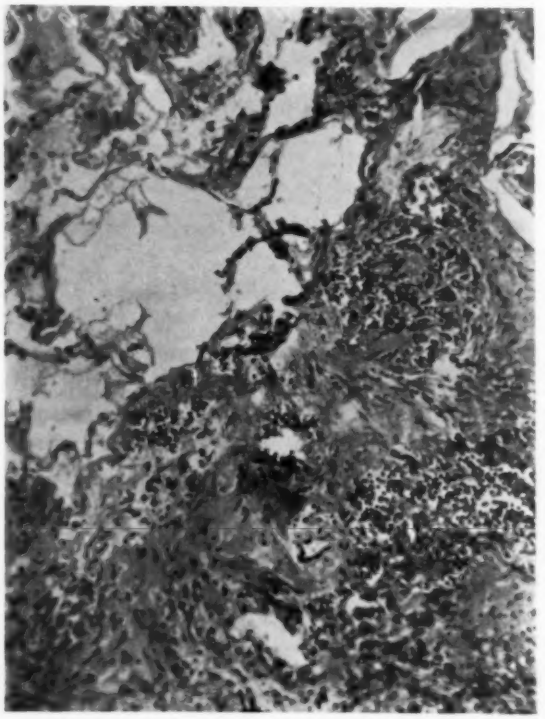

FIG. 4

Figure 2 shows the lungs of the same patient more than a year later after a short stay in a sanatorium. He is still alive, still able to get about, and his sputum still contains fungi. Note the chronic, slowly progressive clinical picture, with characteristic roentgen appearances most nearly resembling those of chronic fibroid tuberculosis. Two other men were similarly affected on the same farm at the same time and made a complete recovery. A man at the neighbouring farm died of a similar condition —no post-mortem examination was done as it was before any case had been referred to me. This illustrates my first case and is accordingly described first, although it is an advanced and chronic case.

Figure 3 is the roentgenogram of the lungs of a patient, aged forty-five, who was admitted in a grave state of ill health in April, 1932, and died in 1934. Tuberculosis was suspected, but never confirmed roentgenologically or bacteriologically. The lungs show the characteristic appearances of fungous infection. A post-mortem examination revealed a voluminous lung with thickened pleura containing numerous bullae. All areas of the lung showed acute congestion and edema and yielded a frothy blood-stained exudate when squeezed. There was evidence of acute bronchitis in the main bronchi.

Figure 4 illustrates a section of the lung shown in Figure 3. Note the emphysematous and ruptured alveoli with acute congestion of the vessels and much patchy fibrosis. On culture they yielded yeast-like cells, long-chained streptococci, *Micrococcus catarrhalis*, and post-mortem anaerobic bacilli. The silica content was 0.15 per cent of dried lung—i.e. within the normal limits.

Figure 5 is the roentgenogram of the lungs of a farm laborer suspected of phthisis. His symptoms dated from haying time and his sputum contained aspergilli. He was given potassium iodide. He rapidly lost his cough, and then discontinued treatment. He came to see me again

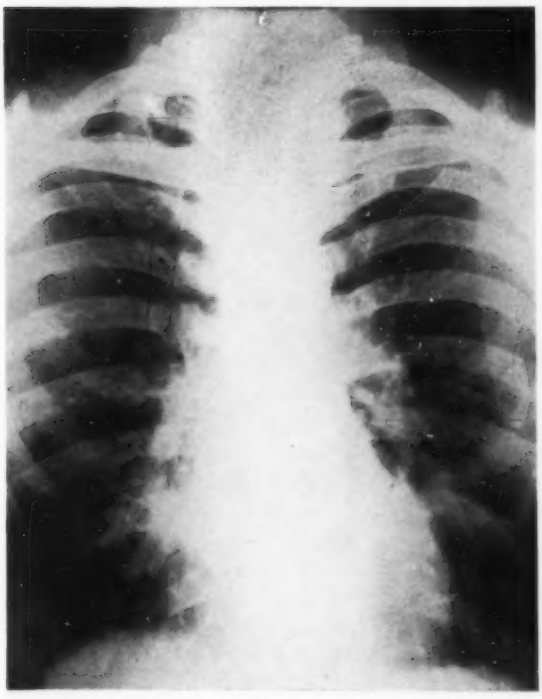

Fig. 5

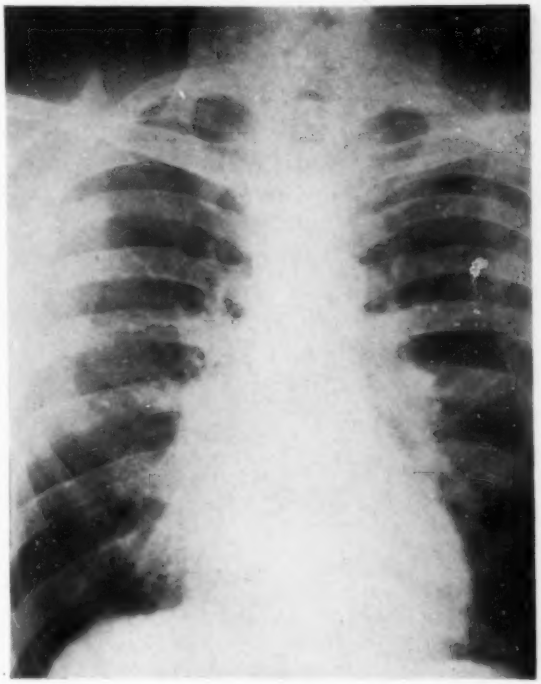

Fig. 6

by request a year later, and Figure 6 shows his lungs at that time, when cough and scanty sputum had returned. This roentgenogram shows a dual picture: the exaggerated linear markings of healing or chronic cases and the mottling of an active infection. Note in particular the emphysematous condition seen at the bases. The sputum yielded cultures of *Aspergillus*, *Penicillium* and *Mucor*.

TYPE 2. THE MYCOSIS OF GRAIN WORKERS

Cultures from the sputum of workers with mouldy grain show a marked predominance of *Penicillium* species. Castellani[8] has described one case of broncho-penicilliosis occurring in a Serbian soldier in the World War. Threshers quite frequently have to stop work because they get asthma or acute dyspnea from the dust. They get better as soon as they are in clean air. I believe that this temporary disturbance is due to mechanical interference which is soon dealt with by the expulsive action of the cilia. Some men, however, are not affected at the time, but get a sudden attack of asthma and acute dyspnea

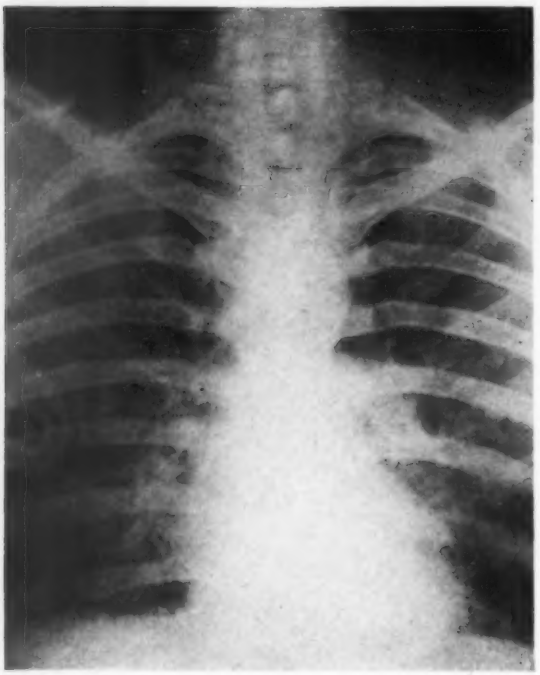

Fig. 7

forty-eight hours or more after handling mouldy grain, and their distress continues for a few days and gradually disappears. Roentgenograms of these patients do not show the fine mottling characteristic of the hayworker's chest; they show exaggerated reticular markings and striation, peribronchial thickening, increase in hilar shadows and some enlargement of hilar peribronchial glands.

I have seen a number of such cases and on the strength of the roentgenograms have collected the sputum and isolated microfungi of *Penicillium* species.

Figure 7 is the roentgenogram of the lungs of a farmer, aged thirty-four, who had threshed mouldy oats on January 12, and suffered from sudden dyspnea about January 23. The oats and the sputum were cultured in parallel and both grew the same fungi (*Penicillium*) in forty-eight hours at 37° C. His film, shows a diffuse mottling distributed throughout both lungs with some patches of emphysema. Intradermal tests were conducted in this case from solutions prepared from subcultures of the fungi isolated from the sputum and the oats. These were definitely positive to *Penicillium* in both solutions. Patient recovered on iodide therapy. It is worthy of mention that the penicillia present a definite problem, there being over 600 named species (Thom).

TYPE 3. THE MYCOSIS OF SOIL WORKERS

Workers with manure and soil are chiefly infected with *Mucor*. The fungi belonging to genus *Mucor* Micheli (1729) are associated with horse dung and soil and are rarely pathogenic. Broncho-mucormycosis has been described by Castellani,[8] and Lucet and Costantin,[19] and produced experimentally by Lucet and Costantin. I have isolated *Mucor* as the preponderating fungus in 3 cases which have certain features in common. All the patients were over fifty and all had the characteristic cough, periodic slight fever, night sweats, loss of weight and occasional hemoptysis usually associated with tuberculosis; but no tubercle bacilli were found on repeated examination, and the roentgen appearances do not suggest pulmonary tuberculosis. In each case the symptoms lasted for several years, without any marked variation until

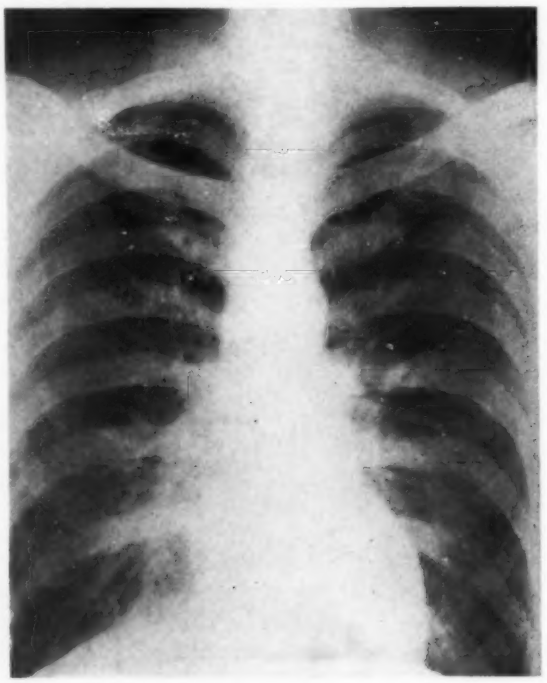

Fig. 8

fungicide treatment was started. Roentgenograms show a marked exaggeration of the peribronchial shadows, suggestive of bronchiectasis, and the bases have the ground-glass appearance associated with asbestosis.

The appearances are well shown in Figure 8, which is a roentgenogram of the lungs of a gardener who had had an excision of the knee joint for tuberculosis and therefore worked in greenhouses. He suffered from cough and hemoptysis, but repeated examination of the sputum failed to reveal the tubercle bacillus. It showed, however, a pure growth of *Mucor racemosus*, a fungus which thrives in greenhouses. I can find no previous record of infection of the lung by this fungus, but Brumpt[3] records this fungus as very virulent in animals, quoting its association with the nasal mucous membrane of horses (Vuillemin) and otomycosis (Jakowski, 1888). The patient improved on potassium iodide therapy and an autogenous vaccine, and his sputum is now free from fungi.

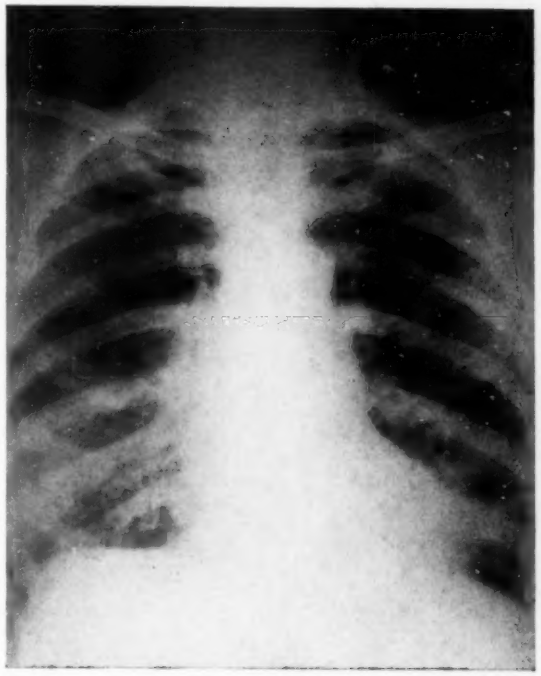

Fig. 9

Type 4. *Botrytis* predominating

A further type which I have encountered is characterized by mixed infection in which *Botrytis cinerea* (a fungus associated with butter, milk [Cummins, Kennelly and Grimes[12]] and decaying vegetation) predominates, but neither of the patients was connected with dairy work. Reference is made by Brumpt[3] and Dodge[13] to the record of a cutaneous condition affecting the arm from which this fungus was isolated.

The appearances are well shown in the roentgenogram (Fig. 9) of the lungs of a married woman, aged sixty-one, who had had a cough for eight years with periodic attacks of dyspnea and hemoptysis. She was suspected of having tuberculosis, but repeated examinations for tubercle bacilli were negative. There was some rasping cog-wheel breathing over the scapula. The sputum yielded a growth of *Botrytis cinerea*, and later also *Penicillium* and *Aspergillus niger*. Her general condition has greatly improved on potassium iodide therapy. Intradermal tests were carried out in this case with three solutions: (*a*) *Botrytis cinerea*, *Penicillium* and *Mucor* sp. mixed; (*b*) *Penicillium* sp. and *Aspergillus niger*; (*c*) *Botrytis* and *Mucor*. There was a strong positive reaction to solution (*b*).

It is one thing to connect fungi with pathological conditions but quite another to obtain scientific proof that the organism is the cause of the disease. A limited number of experiments on animals carried out in the Department of Bacteriology of the University of Edinburgh has shown some fibrosis of lung, but microfungi were not recovered from the post-mortem specimens and the findings were considered inconclusive. Nevertheless, I submit that a case has been made out that goes far to suggest that fungi play a part, perhaps a major part, in these somewhat obscure non-tuberculous conditions of the lungs.

These fungous infections can be distinguished from pneumoconioses by the following considerations: (1) the occupational history of the case, i.e. risk of infection; (2) mode of onset—early acute and sudden dyspnea in bronchomycosis contrasted with the gradual onset after prolonged exposure to silica dust; (3) silicotic lungs in the later stages frequently show areas of coalescence and consolidation, and often develop tuberculous cavitation.

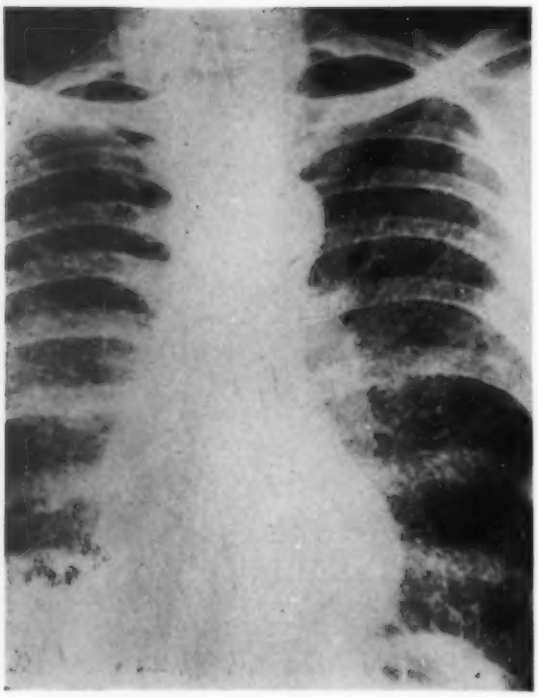

FIG. 10

FIG. 11

MYCOSIS IN HEMATITE IRON-ORE WORKERS

It is of interest that I have found similar appearances in the lungs of hematite iron-ore workers. Men who work many years in the mines show a roentgenogram as in Figure 10, a characteristic snow-flake

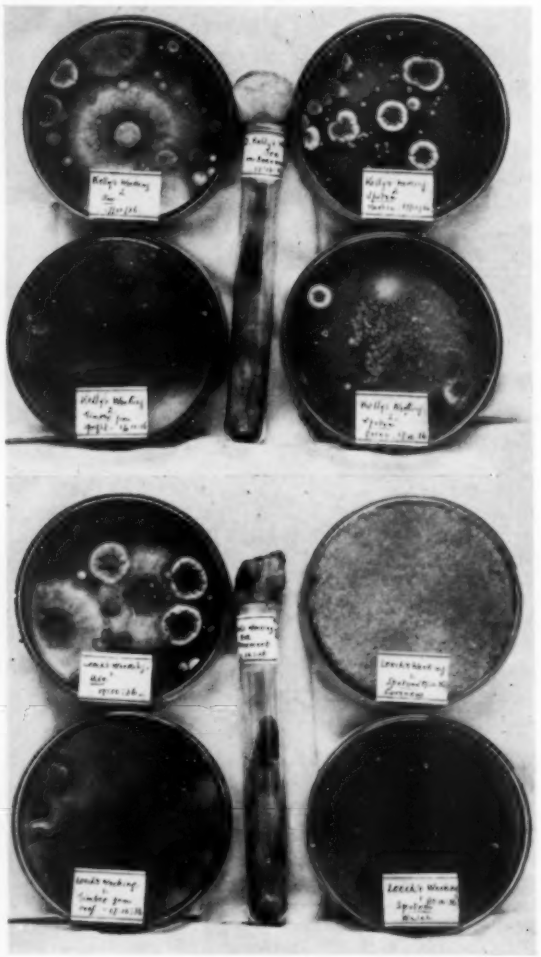

FIG. 12

mottling that closely resembles silicosis and which I had previously associated with the radiopacity of the hydroxide of iron in colloidal suspension; an opinion shared by Collis,[10] Cooke,[11] Kettle,[17] and Stewart and Faulds.[28] This man died from malignant disease of the stomach; yet post-mortem examination of his lungs revealed normal lung and not silicosis nor the *red* lung (Fig. 11 unstained) of the hematite iron-ore worker.

TABLE I

SUBCULTURES FROM CULTURE PLATES

Working	Air	Timber	Ore	Sputum
Leech's Mean temp. 64° F.	1. *T.l.* 2. *T.l.* 3. *T.l.* 4. *G.r.*(*P.*)	1. *T.l.* 2. *T.l.* 3. *T.l.*+*M.r.* 4. *P.*sp.+*M.r.*	1. *P.*sp.+*M.r.* 2. *P.*sp.+*M.r.*	*Case 1. J.W.* 1. *T.l.* 2. *T.l.*+*M.r.*
				Case 2. J.C. 1. Hy.m. 2. *M.*sp. 3. *M.*sp.+*T.l.*
Kelly's Mean temp. 57° F.	1. *T.l.* 2. *T.l.*+*P.*sp. 3. *T.l.* 4. *T.l.* 5. *T.l.*	1. *M.r.* 2. *P.*sp. 3. *T.l.*+*Gl.ros.* 4. *M.r.*	1. *M.r.To.*sp.*P.*sp. 2. *M.*sp.+*P.*sp.	*Case 3. H.D.* 1. *T.l.* 2. *T.l.* 3. *T.l.* 4. *T.l.*+*Gl.ros.* 5. *Gl.ros.*
				Case 4. L.M. 1. *P.*sp. 2. *P.*sp. 3. *T.l.* 4. *T.l.* 5. *T.l.*
Armstrong's Mean temp. 64° F.	1. *Ha.*sp. 2. *S.*sp. 3. *Hyphae* 4. *A.n.*+*G.r.* 5. *A.h.*	1. *M.r.*+*C.a.* 2. *P.*sp.+*Gl.ros.* 3. *P.*sp.+*M.r.* 4. *P.*sp.+*M.r.*		*Case 5. A.A.* 1. *T.l.* 2. *T.l.* 3. *T.l.*
Graffen's Mean temp. 58° F.		1. *M.r.* 2. *T.l.* 3. *M.r.*	1. *P.*sp. *A.*sp. *G.r.*	*Case 6. J.G.* 1. No growth. 2. *P.*(red reverse). 3. *M. mucedo* (?) 4. *S.*sp. 5. *M.*sp.+*P.*sp.

A. = *Aspergillus*
A.h. = *Aspergillus herbariorum*
A.n. = *Aspergillus nidulans*
C.a. = *Cephalosporium acremonium*
Gl.ros. = *Gliocladium roseum*
G.r. = *Graphium rigidum*
Ha. = *Haplographium*
Hy.m. = Hyaline mycelium
M.r. = *Mucor racemosus*
P. = *Penicillium*
S. = *Saccharomyces*
To. = *Torula*
T.l. = *Trichoderma lignorum*

All plates except Graffen's air, contained *Trichoderma lignorum* and *Mucor racemosus*.

Through the courtesy and generous co-operation of the Barrow Haematite Steel Co., I have made some investigations on the presence of fungi in the sputum of miners and in the air, timber and iron-ore of the mines themselves. Specimens were collected in the mine by myself directly on culture plates, with the utmost care to avoid contamination. Specimens of the sputa of men from the workings in which

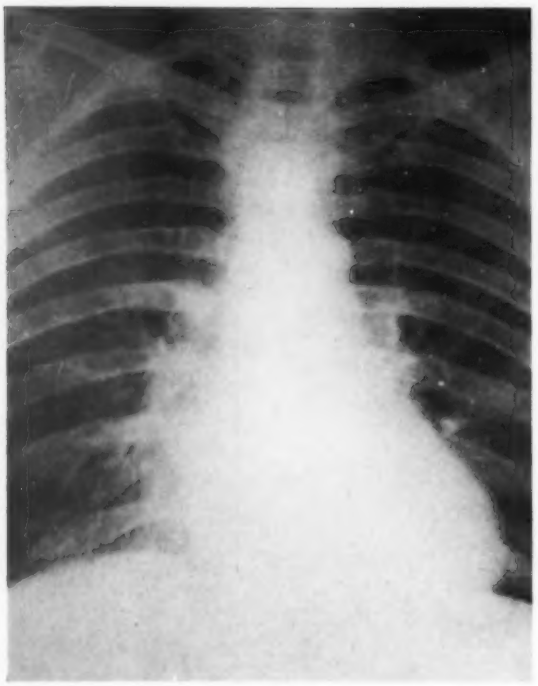

FIG. 13

the plates were inoculated and exposed were taken in the mine captain's office before these miners went below to work—with due precautions. Roentgenograms of their chests were taken later. The resulting culture plates, as illustrated in Figure 12 and identified in Table 1, show an interesting correspondence between the fungi in the air, timber or ore, and those in the sputum of the men working in the areas from which the specimens were taken. *Trichoderma lignorum* (a fungus found in rotting timber) and *Mucor racemosus*, which I have recently grown at 37° C., were found in all the specimens and accordingly not selected in every case for subculture; but the plates exposed to the air where a soap spray was used to lay dust just after firing a shot were found to be sterile, exhibiting the efficiency of this method as a dust laying agency as employed by this mining company.

The occurrence of fungi in mines is mentioned by Pancoast and Pendergrass.[25] Towey[30] has recorded pulmonary symptoms in men working amongst mouldy timber (maple).

Figure 13 is a roentgenogram of the chest of a hematite iron-ore worker of good physique and good health and with a chest expansion of 4 inches. He had worked eighteen years in the mines and his sputum showed fungi of the kind found in roof timber where he worked. This is typical of the chests of the series of men I examined. I have found a similar roentgenographic appearance of the chest in surface workers at the mines, but it is of note that many of these men have been farm servants previous to their employment in the iron-ore industry.

Recently a man died at the age of sixty after fifty years' work in the mines. He had had to stop work because of shortness of breath, and had been granted compensation as suffering from silicosis. No tubercle bacilli had been found in his sputum. At autopsy both lungs were voluminous, and the right pleura had some small fibrous adhesions. They were dark blue-grey, and did not look like the lungs of a hematite miner. Section revealed edema and conges-

FIG. 14

tion and some fine nodular fibrosis which did not resemble either the nodular fibrosis of silicosis, or the generalized massive fibrosis of hematite, though two small silicotic nodules were found, one of which is illustrated in Figure 14. *Syringospora albicans* (Robin) Dodge was isolated from his lungs post mortem. Figure 15 illustrates the roentgen appearance of this chest six months previously—note the tendency to some coalescence in right upper and midlung fields.

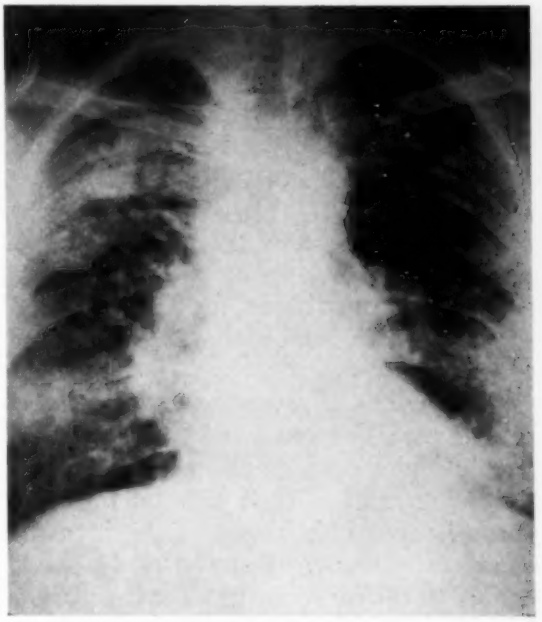

Fig. 15

Here was a case that presented all the roentgenological appearances of silicosis, but sections of the lung and the general pathological and chemical analysis disproved the diagnosis. One cannot help suspecting that this also was a case of fungous disease.

As already suggested, I believe that fungous infection is frequently associated with dust diseases. Furthermore I believe, as previously stated as a result of my experimental work, that there are periods of pathogenicity of some fungi which are generally non-pathogenic. I therefore asked a local practitioner to put half-a-dozen pensioned silicotic miners on intensive potassium iodide therapy. Within three weeks all showed marked relief of the dyspnea and improved general condition; so much so that one who had been confined to his chair for six months ran up-stairs just to show the doctor what he could do. A limited number of intradermal tests have proved positive to solutions prepared from *Trichoderma lignorum* and *Mucor racemosus* mixed; further tests are in progress.

Clinical results such as these are very suggestive that fungi do play a part in dust diseases, and that bronchomycosis may play some part in the vexed and vital problem of silicosis, a subject on which Barclay is at present doing valuable experimental work. Campbell believes that the mottling seen roentgenologically is due to the collapse of the alveoli caused by occlusion of the bronchioles. Barclay, however, suspects that the fungi interfere with the expulsive action of the cilia. Perhaps they act by sensitizing the lung: when fungi invade the lung they break down its defences against the mechanical injury by the particles and the biochemical action of the silica. The fungi may perhaps also set up an allergic condition. Intradermal tests now in progress support this view. It may be that there is a biological as well as a biochemical and mechanical factor in the chain of events which leads to the condition we call silicosis. I am inclined to think that in association with the fibrosis of silicosis it is the fungous infection that counts rather than any particular species of fungus.

In arriving at a diagnosis of bronchomycosis I lay stress on the following points:

(1) Occupational history.
(2) Source of infection.
(3) Mode of onset.
(4) Clinical findings—dyspnea out of all proportion to other symptoms.
(5) Finding of fungi in sputum in the absence of tubercle bacilli on repeated examination.
(6) Roentgenological appearances—importance of recognizing early stage.
(7) Reaction to intradermal tests.

(8) Tendency to recovery on potassium iodide and vaccine therapy, and here I should mention the inadvisability of delaying therapeutic measures until the pathogenicity by animal experiments is established.

It must be evident from a consideration of the cases recorded that the incidence of some of the dust-borne fungi, under certain conditions, should be considered an occupational risk.

I have confined my remarks to some of the cases which have come directly or indirectly under my own observation and do not profess to have dealt with the different types of mycotic infection of the lung, as described by many others. It has been impossible to adhere strictly to the roentgenological side of this subject; the mycological and clinical aspects are so interwoven with this that without some mention of them the subject would be pointless.

In conclusion, I am aware there is much in this paper which is open to criticism. I welcome criticism if it will arouse interest in a subject which has occupied the majority of my spare time during the last three years, and stimulate others with greater opportunities than myself to pursue this work which I am convinced is of paramount importance.

I should like to record my thanks to those who have supplied me with material for this investigation, but in particular my thanks to Dr. Faulds, the County Pathologist for Cumberland who has supplied me with pathological sections, and whose discovery of the fungus in my first case initiated this work; to Dr. Barclay who has urged me ever onwards; to Professor Ramsbottom and Miss Stephens (of the Natural History Museum, South Kensington, London) who have identified the vast majority of our fungi; to Miss Hoggarth in particular, my roentgenographer in Ulverston, who has spent endless time in preparing reproductions and the text, and the media on which to grow our specimens (the fact that no group of media has had one single contaminant speaks volumes for her thoroughness); and lastly my appreciation of the high honour that has been conferred upon me by our president, Dr. Christie, in inviting me to produce this paper.

SUMMARY

In this paper is described the occurrence, in the Northwest of England, of microfungi in the sputa of a number of persons engaged in agriculture, who had handled mouldy hay, grain, soil or decaying vegetable matter, and who suffered from respiratory symptoms of which distressing dyspnea was the most marked, and who presented certain roentgenographic appearances in their lungs. A plea is made for the early recognition of this condition of bronchomycosis, the onus of which recognition must rest largely upon the roentgenologist, for at this stage of the disease it yields readily to therapeutic measures mentioned.

Furthermore the occurrence of a similar condition in hematite iron-ore workers, and a possible link in the chain of events leading to silicosis is considered.

It is believed that the presence of dust-borne microfungi involves an occupational risk.

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THE NORMAL SKULL

FROM A ROENTGENOLOGIC VIEWPOINT*

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AS THERE are no two skulls exactly alike, we are immediately confronted by the question: What does a normal skull look like? The answer can only be: One in which no abnormality can be demonstrated. But this does not suffice, because the answer begs another question: What constitutes an abnormality? An abnormality is any variation which, in the light of our present knowledge, can be associated with some clinical manifestation. This means that as time goes on and our store of knowledge increases, many of the so-called normal variations which include benign calcifications, will no longer be classed as such, but will be recognized as the result or perhaps the cause of some physical or chemical abnormality.

The skull is developed in a remarkably complicated manner and it is really amazing that more abnormalities are not found. Nearly all the bones are derived from several centers of ossification. The sphenoid, for example, usually begins with five such centers, and furthermore approximately half of the skull is of membranous origin and half originates in cartilage. This is well shown in Figure 3. From this chart it can be seen that the bones of membranous origin are those forming the calvarium, while those derived from cartilage form the base with the exception of the membrana tympani and squamous portion of the temporal bone, the hamulus of the pterygoid process, and the occipital bone below the superior nuchal line.

The diameters of the normal skull vary considerably. Broca gives the following figures for the average skull:

Mean	*Males*	*Females*
Length	182 mm.	174 mm.
Breadth	145 mm.	135 mm.
Height	132 mm.	125 mm.

However, it must not be gathered from this table that any skull with measurements greater or less than those quoted is, ipso facto, an abnormal skull. Other factors must be carefully considered, chief among which is the clinical history. But generally speaking, any skull which varies much from the average set by Broca may well be viewed as probably abnormal until proved otherwise. The shape of the skull is protean, but all types can be classified within three groups, which are called brachycephalic, mesocephalic, and dolichocephalic. In order to place a skull in one of these groups, its cephalic index must be determined by use of the formula devised by Retzius, which is:

$$I = \frac{\text{greatest internal breadth} \times 100}{\text{greatest internal length}}$$

(measurements in centimeters). If I is found to equal a number between 70 and 80, the skull is mesocephalic; if more than 80, it is brachycephalic, and if less than 70 it is dolichocephalic.

It might be of interest to note that the brachycephalic skull is most common among the yellow races, and from a surgical point of view, the dolichocephalic skull is of interest because the fissure of Rolando is apt to be found slanting backwards a little more than is found in the shorter heads. The shape of the skull can vary considerably within each of the three groups, and these shapes have been given more or less descriptive names, such as turricephaly or turret-shaped head, oxycephaly or pointed head, scaphocephaly or long and boat shaped, also called scaphoid head, plagiocephaly or slanting asymmetry. Most of these shapes are really not strictly within the realm of normality because they are the result of some external

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force or a more or less asymmetrical synostosis cranii. As a rule, unless the form of the head is particularly striking, it can be classed as normal provided there is no clinical symptomatology that might be ascribed to its shape.

while if the angle is more than 5 or 6 degrees greater than the average, the skull is platybasic. The variations of the basal angle within reasonable limits of about 5 to 10 degrees need not in themselves indicate an abnormality, for such variations

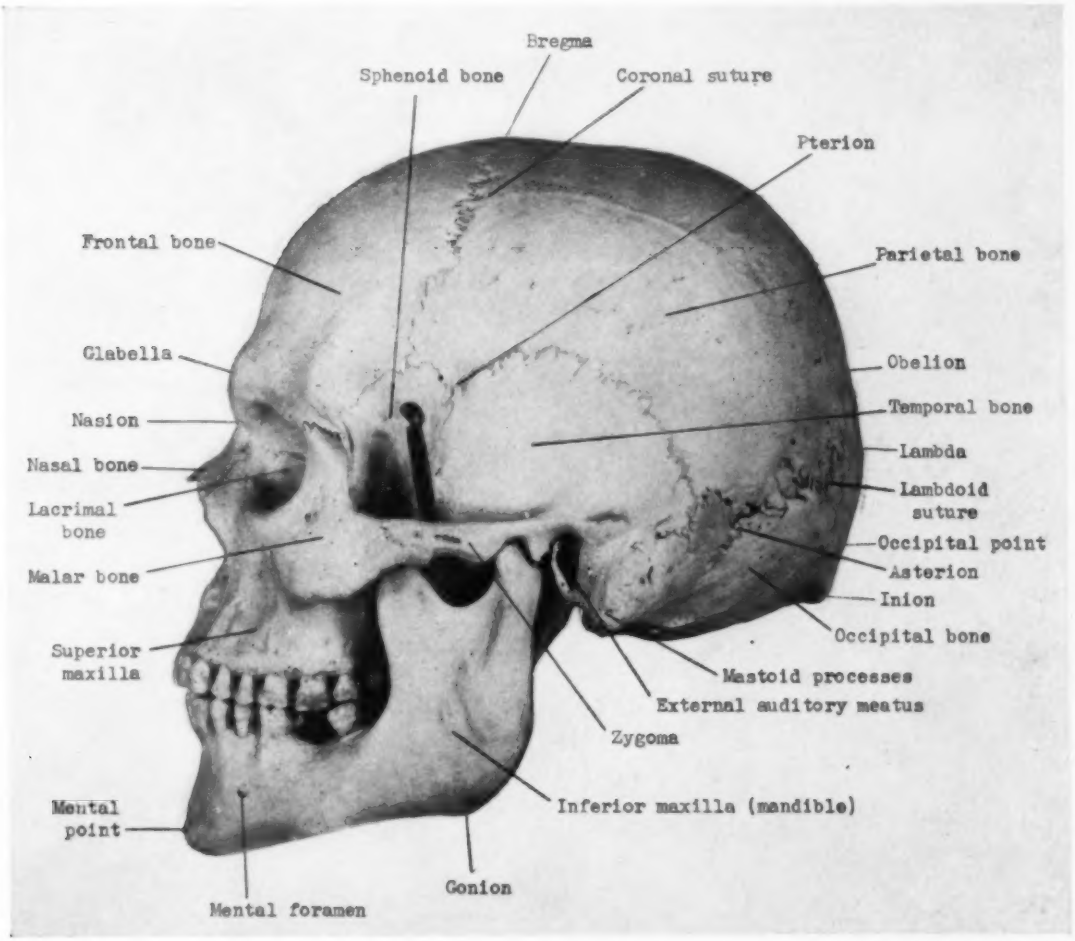

Fig. 1. External anatomy of the cranium. (Mounted skull by courtesy of Clay-Adams Company, New York City.)

The basal and facial angles might be briefly considered. The basal angle of Welcker is really a measure to determine the shape of the base in relative terms, and is the angle subtended by a line drawn from the nasion to the tuberculum sellae, and a line from the anterior margin of the foramen magnum to the tuberculum sellae. This angle is usually found to be about 134 degrees; if it is much less, the skull may be considered to have a kyphotic base,

are often encountered as a result of some growth disturbance of childhood, probably due to a more or less obscure endocrinopathy, and if later the patient has become endocrinologically balanced, the shape of the base has a historical interest only. The basal angle will be markedly altered in cases of synostosis cranii in which most of the sutures are involved. This would be apt to produce a shortened base and a reduction of the basal angle. On the other

hand, a nutritional disturbance in childhood could easily allow an invagination of the base with a considerable increase in the basal angle. Rarely will the angle become less after growth has ceased, although occasionally in the case of adults with some form of malacic disease such as osteitis deformans, there may be a softening of the bones of the base with subsequent invagination, and an increase in the basal angle.

The facial angle, or angle of Weisbach, is the angle formed by two lines drawn from the mental point, one to the nasion, the other to the anterior margin of the foramen magnum. This angle averages about 73 degrees, and would indicate an average or orthognathic skull. If the angle were found to be less, by more than a few degrees, the skull would be considered as prognathic in type, and an increase in the angle of 5 to 10 degrees would indicate an enognathic skull. Variations, unless marked, are of no pathological significance. If the angle varies more than 5 to 8 degrees

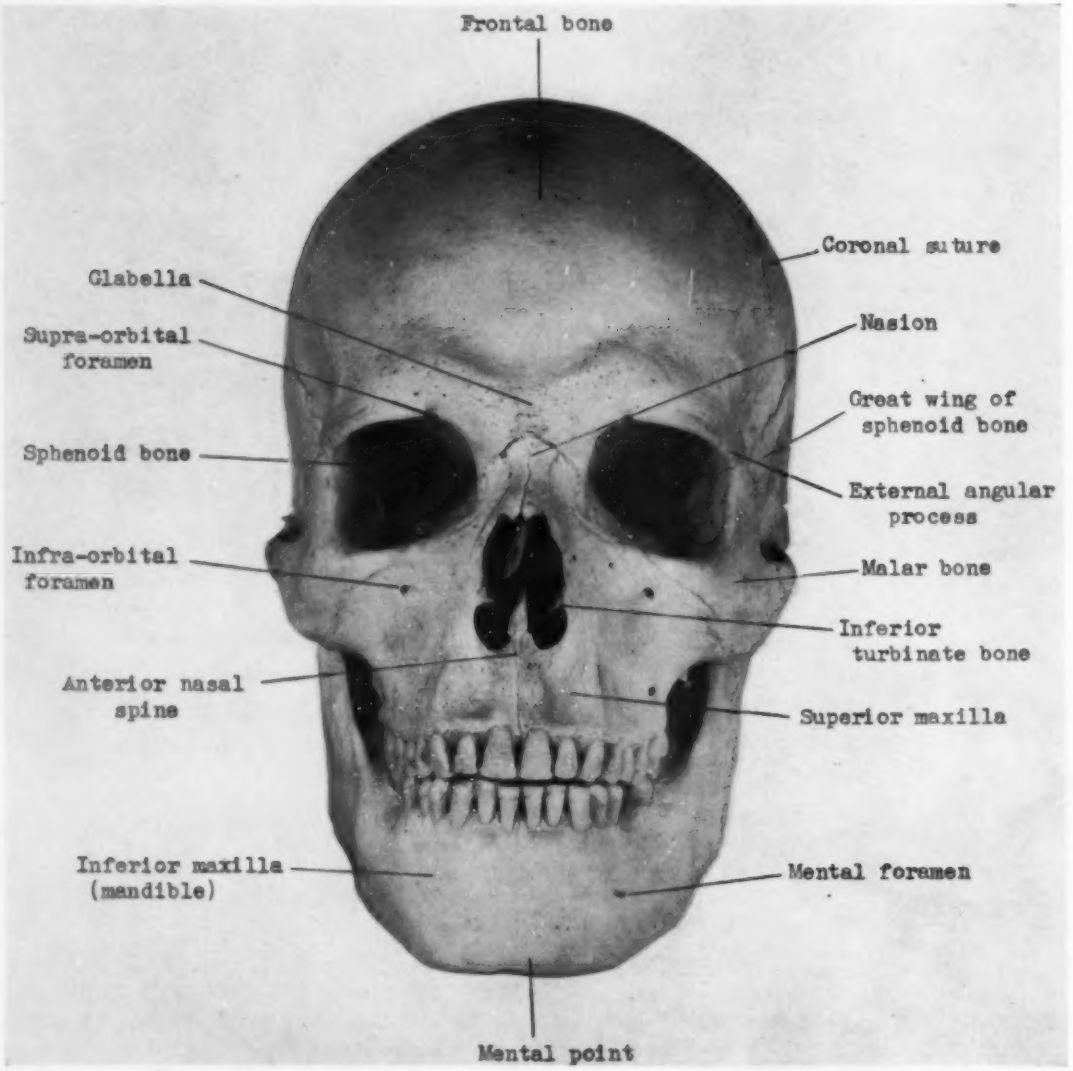

FIG. 2. External anatomy of the skull. Frontal view. (Mounted skull by courtesy of Clay-Adams Company, New York City.)

on the side of prognathism, it would be likely to be associated with some definite clinical syndrome.

The two halves of the average skull will be found, upon close inspection, to be more or less asymmetrical. This asymmetry may be general or confined chiefly to special structures. In either case, unless it is marked, it usually can be disregarded. It is well to remember that the skull grows fairly rapidly for the first seven years of life, followed by a period of rather slow enlargement until puberty, after which full size will be rapidly attained. According to the recent studies of Hrdlicka, it is not uncommon for a skull to continue to grow slightly even into the sixth decade. These normal irregularities in growth should be carefully considered when evaluating any changes which might be considered abnormal. It should also be noted that the posterior portion of the average skull enlarges but little after the age of ten to twelve years, whereas the anterior portion may continue to grow until the age of about twenty-five years.

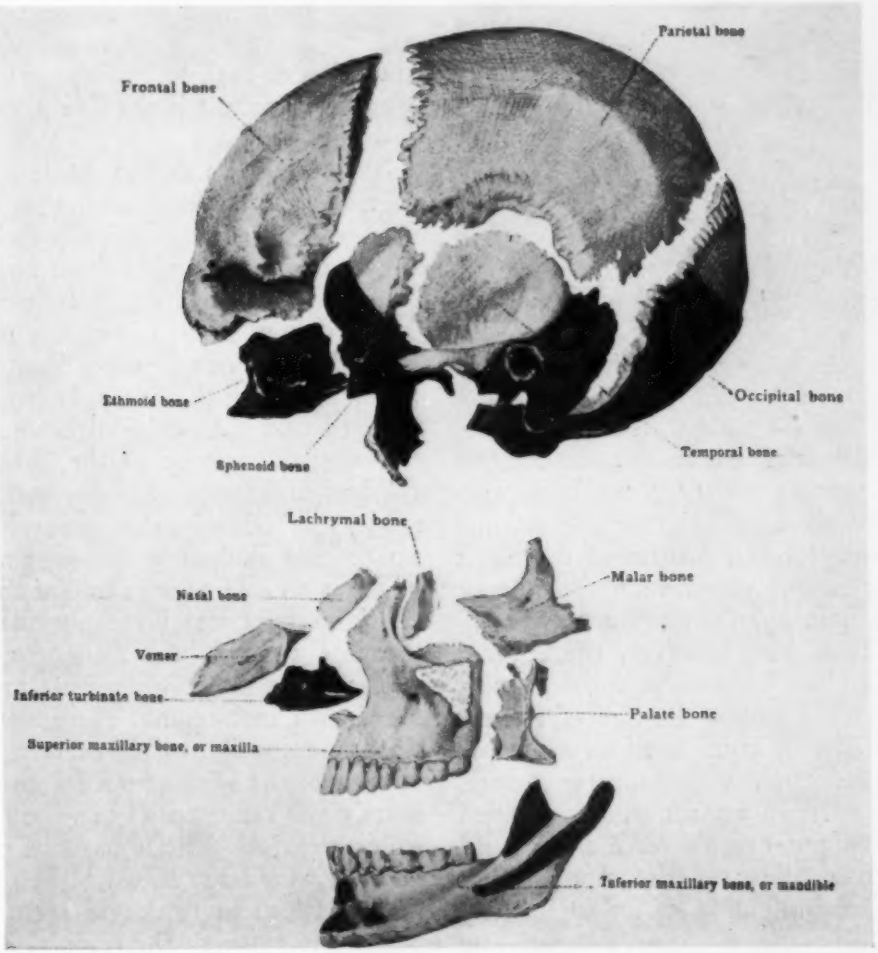

Fig. 3. The lightly shaded bones are of membranous origin, while those in black originate in cartilage. (Illustration taken from Geschickter and Copeland, "Tumors of Bone," American Journal of Cancer, New York City.)

The sutures undergo union in a most irregular and unpredictable manner, but as a rule, those of the base are closed at the age of about one to two months, with the

Fig. 4. A typical example of dolichocephaly.

exception of the occipitosphenoidal suture, which usually unites between the ages of about thirteen to twenty years. It is practically impossible to designate any normal closure times for the sutures of the vault because it is not uncommon for one or more to remain open throughout one's entire life. As a rule, however, the coronal suture will close before the third decade, but if it unites before the age of twenty years it might be considered as a premature closure. Such a premature closure, unless it results in an abnormally shaped head, is of no great significance, but should be noted, particularly if the union is solid, as a possible indication of an underlying endocrine imbalance or hypercalcemia. The sagittal suture usually remains open a few years longer than the coronal, and like the lambdoid may remain open indefinitely. Any of the sutures of the vault may include one or more supernumerary bones known as wormian bones. This is more common in the lambdoid suture which not infrequently contains several of these bones. It is important not to confuse wormian bones with fractures. This is not likely if the characteristic configuration of the suture can be followed completely around the bone, not a difficult feat with good stereoscopic films. Occasionally, the suture line in the outer table of the skull will not exactly coincide with its counterpart of the inner table; this will result in a double line which at times may simulate a fracture running through the suture. This anomaly is not infrequent and can as a rule be readily recognized by the fact that there are no serrated contiguous edges corresponding to each half of the suture, which would be present if the line were due to a fracture.

The thickness of the vault varies considerably within normal limits. It is difficult to state dogmatically what these limits are, but roughly from about 3 to 7 or 8 mm. would include most normal skulls. In any given skull it is rather uncommon to find the bones forming the vault to be all of the same thickness. It is quite common to find the occipital bone thin, particularly the portion of the bone covering the occipital fossae. The parietal bones are subject to considerable normal variation up to and including actual fenestration, which is an interesting familial characteristic. The temporal bone not infrequently presents a small, usually single, enostosis of the inner table. This must not be confused with an osteoma. The enostosis upon close examination will be seen to be formed of bone of the same structure and approximately the same density as the bone from which it arises. The squamous portion of the temporal bone is apt to be quite thin. Its variations in thickness are quite comparable to those of the occipital bone.

The horizontal portion of the frontal bone often presents marked irregularities in the form of grooves and knobs. These irregularities are important to note, particularly if the case is potentially surgical. It is quite obvious that if the frontal cerebral lobes are raised from an irregular bed it will be very difficult to replace them in the exact relationship that they previously occupied with the bony irregularities, an important maneuver if a good result is to be anticipated. The vertical portion of the frontal bone should be fairly smooth in out-

line and of even thickness to be considered normal. It is on this portion of the frontal bone that one so often encounters a more or less diffuse and irregular enostosis, most common in the female skull, and probably due to an underlying endocrine dyscrasia. It is at times quite difficult to determine whether a calvarium under examination is or is not normal. One of the most important things to note in making such a determination, is the appearance of the bony structure and the calcium content. A somewhat "washed out" appearance with a tendency toward a mottled pattern would lead one to suspect halisteresis, but if the tables are thin and the diploe plentiful, the bones may be of a diminished density which is more apparent than real. In such a case a careful examination of the cortex will usually permit a differentiation between true and apparent demineralization, and in the final analysis a true generalized demineralization will not be confined to the bones of the skull. On the other hand, a slight thickening and increased bony density would lead to the suspicion of the presence of an hypercraniosis. The changes due to definite pathological conditions would rarely be confused with the normal.

Intracranial calcifications, in the present imperfect state of our knowledge, are termed physiological or pathological. Those which are considered physiological are the lime deposits so often encountered in the pineal gland, in the meninges, usually seen in the falx cerebri, in the margins of the diaphragma sellae, in the free edges of the tentorium cerebelli, posterior to the dorsum sellae, and in the knees of the choroid plexuses. Calcification in these structures is quite common after about the twenty-fifth year when they will be found in approximately the following percentage frequencies: pineal 55 per cent, diaphragma sellae 14 per cent, falx cerebri 9 per cent, choroid plexuses 8 per cent, tentorium cerebelli 6 per cent, and dura mater 6 per cent.

The various deposits of calcium are of importance merely from the point of view

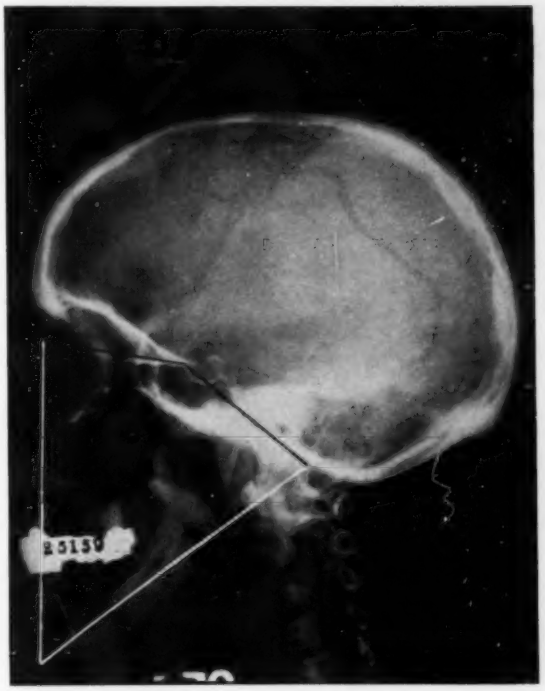

Fig. 5. The basal angle is formed by the black lines. The facial angle is indicated by white lines.

of locating the structures in which they occur. This is particularly important in the case of the pineal gland which is so frequently displaced in the presence of intracranial pathology. The normal position of the pineal body can easily be determined by use of the charts devised by Vastine and Kinney, which were so ably corroborated by Dyke. This diagnostic possibility was mentioned by Earl in 1913, and more explicitly by Naffziger in 1925. A shift of the pineal gland from its normal position is a very important diagnostic factor. It must, however, be borne in mind that the pineal body may be apparently shifted slightly in the sagittal plane as determined by the charts, if the skull is markedly dolichocephalic or brachycephalic, without its being of any significance, so that the shape of the head must be carefully considered when evaluating the importance of a slight pineal shift. Calcium deposits in the falx cerebri may be of importance in showing whether or not the falx occupies its normal midline position. The deposits are situated

Fig. 6. A single non-pathological enostosis of the inner table of the temporal bone.

usually on the side of the falx and are roughly triangular in shape, with the apex placed laterally. These calcifications not infrequently involve the walls of the sagittal sinus and so give us an idea of its size. Lime deposits in the margins of the diaphragma sellae should be carefully differentiated from linear deposits often seen in the walls of the cerebral portions of the carotid arteries, which are of course an indication of arteriosclerosis. In good stereoscopic films such a differentiation is not difficult. Calcification in the glomus of the choroid plexus, which is the portion of the plexus situated at the juncture of the body and temporal horn of the lateral ventricle, may be seen on one or both sides and may normally vary from about a centimeter in diameter to less than a millimeter. These deposits are as a rule of no apparent clinical significance but occasionally they may indicate the presence of a papilloma or a cholesteatoma, so that such possibilities must not be lost sight of.

It is my personal feeling that these so-called benign deposits are considered of no significance because we are not yet clever enough to determine why they form. It seems highly probable that as our knowledge of calcium metabolism increases, such deposits of lime will prove to be an indication of some underlying systemic disturbance and therefore not normal as they are now considered to be. Any intracranial calcification other than those mentioned should be viewed with alarm.

The formation of the air sinuses is so variable that it represents a distinctive pattern for each skull, so distinctive in fact that it is an excellent method of individual identification. Most anatomical variations occurring in the sinuses are of no clinical significance unless the sinuses become infected, hence even an attempt at describing them would be futile with, however, the following notable exceptions: If the frontal sinuses are very small and remain so into adult life, it seems highly probable that such a lack of development may be associated with some underlying endocrine imbalance, and by the same token, if the frontal sinuses are large and bulge forward, it is usually an indication of some acromegaloid tendencies. But it should be noted that this overdevelopment is not at the expense of the cranial capacity. At times we find the frontal sinuses developed asymmetrically, and usually accompanied by a supra-orbital ethmoid cell development, all of which is at the expense of the cranial capacity. This condition is frequently accompanied by an overdevelopment of the petrous pyramid on the same side, and perhaps a unilateral thickening of the calvarium. Such an asymmetrical formation is an indication of an asymmetrical cerebrum, and was described together with confirmatory encephalographic findings by Dyke, Davidoff and Masson. The cerebral hemisphere on the side of the overdeveloped sinuses is smaller than its counterpart, and will usually be found to be agenetic.

The circulatory channels, which can almost invariably be recognized on the inner

table of the calvarium and through the diploe, are worthy of careful study. It is, as a rule, possible to differentiate between the venous and arterial channels if one bears in mind the fact that the arterial channels usually course upward and backward, and that they tend to taper out to terminal points, and are smaller in diameter than the venous channels. It would be futile to give definite figures in millimeters above or below which the channels would be considered abnormal, but the average is about 1 mm. The venous channels are more tortuous and irregular in their distribution. They tend roughly to course upward and forward and to maintain a fairly constant caliber, which is, as a rule, slightly greater than the arterial channels. The diploic channels, the so-called veins of Brechet, are apt to be quite large, 2 or 3 mm. in diameter, particularly if the diploe is plentiful. The diploic veins are usually grouped according to their drainage, into the frontal, temporal, anterior and posterior parietal systems. The veins draining these systems or plexuses are the anterior diploic vein which drains into the supra-orbital or ophthalmic vein, the anterior temporal diploic vein which drains into the sphenoparietal sinus or deep temporal vein, the posterior temporal diploic vein which usually drains into the mastoid emissary vein, and the occipital diploic vein which drains eventually into the torcular Herophili or lateral sinus. It is not uncommon to find a fairly large diploic veniplexus of a more or less stellate shape in the posterior parietal system which may be unilateral or bilateral without being of any clinical significance. These diploic veins, being very thin-walled structures, often show localized enlargements which produce shadows in the film not unlike pacchionian impressions, and may be considered as normal diploic lakes. The true venous lakes or "lacunae venosae" occur in the dura mater adjacent to the longitudinal sinus, and are not to be considered abnormal.

The chief point to be determined in deciding whether or not there is any abnormality in the circulatory channels is whether or not a given area is actually hypervascular. Such an area to be abnormal would be unilateral and would consist of many or even a few channels which would tend toward a racemose configuration with or without a honeycombing of the overlying bone, and as a rule the channels leading to and from this area would be of greater caliber than any corresponding channels of the opposite side or any of the channels in the immediate vicinity. Rarely, bilateral areas of hypervascularity may be encountered. Such a finding, unless most obvious, might make the differentiation between normal and abnormal very difficult. In this connection, however, it must be noted that the channels for the middle meningeal vessels, which course upward to the bregma from the outer tips of the lesser sphenoid wings, may differ considerably on

Fig. 7. The type of frontal air cell development that is significant of an asymmetrical cerebrum.

Fig. 8. Large diploic veins.

the two sides without such difference being of any clinical significance.

Pacchionian impressions are uncommonly seen prior to the age of about twelve years. But in the adult skull they are frequently seen as moderately large or small indentations of the inner table on either side of the longitudinal sinus. There are, as a rule, about three of these impressions on either side of the midline which may be made to seem larger by being in conjunction with dural lacunae. Atypically situated pacchionian indentations may be encountered almost anywhere over the inner table of the calvarium, and can usually be identified by their smooth outlines, normal-appearing surrounding bone structure, and the fact that one or more vessel channels will be seen leading from them. The position of several of the large dural sinuses can be recognized in the film of the skull by the grooves in the inner table overlying them. Those that can be identified are the sagittal (superior longitudinal), the occipital, and the lateral or sigmoid sinus. The chief point to note in connection with these sinus grooves is whether or not they are in their normal locations. Occasionally the lateral sinus will be found above its normal site. Such a finding is, of course, of no clinical significance, but would be of interest to a surgeon contemplating an operation in the posterior fossa.

The convolutional impressions have recently been subjected to a careful scrutiny by Davidoff who has been able to confirm many previously held opinions, and has added some valuable comments. He concludes that the convolutional markings are most plentiful during the time of most rapid brain growth. This corresponds very closely to the characteristics of skull growth as noted before in this article. It is rare to find recognizable convolutional markings prior to the age of one year, and as a rule in the adult skull only a few will be found in the temporal and parieto-occipital regions, usually better marked in the temporal regions if the temporal bones happen to be thin. In determining the normality or abnormality of a given distribution of convolutional impressions, the appearance of the bone is of prime importance. The overlying bone and the interconvolutional ridges must have a well-mineralized appearance to escape the suspicion of pressure atrophy. This is of more importance than the actual number of digitations, which can vary widely within normal limits, depending upon the thickness of the skull. It must not be lost sight of that these impressions are definitely increased in number and depth in the presence of an elevation of intracranial pressure which has been a factor for a few months. There will also be a tendency toward an increase in the number of convolutional impressions in the presence of a hypocalcemia, a condition which can often be recognized by a study of the skull. Lückenschädel, a developmental anomaly of the very young, gives the appearance of markedly deepened convolutional impressions, but would hardly be mistaken for the normal.

The petrous pyramids are important structures to study in determining the normality of a skull. The ridges are often not alike on the two sides so that a study of the bony cortex becomes of prime importance.

It should be clearly defined in order to allay all suspicion of the presence of atrophy. If one ridge is higher than its mate of the opposite side, an asymmetrical cerebrum might at least be suspected, and if one mastoid antrum is seen to be larger than the other, its walls should be carefully examined for evidence of atrophy due most likely to an epidermoid or possible malignant tumor. In this connection it might be noted that any mastoid antrum with a diameter much in excess of 12 mm. should arouse one's suspicion that all is not well.

The structure known as the sella turcica has had so much written about it that it has become, in a sense, almost legendary. It seems to me that a large proportion of the literature is based upon fact, but some may be slightly tinged with wishful thinking. It is not my intention to add to this literature, but in order to undertake a discussion of the normal sella turcica, the expression of some opinion cannot be escaped. Many authors have stated sizes for the sella turcica beyond which the normal must not go. These measurements are in themselves, I believe, largely of academic interest only. It is certainly safe to say that a sella turcica of over 15 mm. in anteroposterior diameter should be viewed with suspicion, and one of 6 mm. or less would be considered small. If the cortex of the bone forming the structure shows any evidence of atrophy, then of course it is abnormal, no matter what its shape. It should be remembered that the apparent size of the sella turcica is only a rough estimate of the size of its valuable contents, the pituitary gland. This gland can find room to expand to some extent laterally, and as the position of the optic chiasm is not always exactly the same, the diaphragma sellae may be slightly arched in some cases.

The shape of the sella turcica varies with every skull, and therefore so does the size. It is possible to work out tables showing the proportionate size of the pituitary fossa and the size of the skull, but this merely gives us an average, which is again of academic interest only. It is true that in many cases of hypopituitarism a small sella turcica will be found, but this is not a one hundred per cent finding. A perpendicular dorsum sellae has been suggested as evidence of intermittent intrasellar pressure. This is possible, but unless we see evidence of atrophy or evidence of repaired atrophy in the form of increased bone density, we must conclude that the dorsum sellae was originally and normally perpendicular. At present it is almost as difficult to define a normal sella turcica from a physiological viewpoint as it is to draw the line between sanity and insanity. My own feeling is that if the sella turcica "physiologically fits" the skull in which it is found, it is normal regardless of its shape or size. This of course makes the clinical findings a prerequisite to such a determination. In attempting to determine the normality of a skull from a physiological point of view, we must not spend all the time contemplating and theorizing on the appearance of the sella turcica. This structure, important as it is conceded to be, is nevertheless only one link in the chain of evidence, and it must be considered in conjunction with the shape of the skull, the relative calcium content and thickness of the bones, the development of the air sinuses, and the amount of diploe. It is at present, and probably always will be, impossible to state in concrete terms how to differentiate between the normal and abnormal appearance of these structures as seen in the roentgenogram. Each skull must be considered as an individual and therefore, at least for some time to come, the personal element must play an important rôle in determining just what is a really normal skull.

SUMMARY

An attempt has been made to discuss the appearance of the average normal skull as seen in the roentgenogram, and to point out some of the variations which might be of clinical significance, and to indicate others which are of no significance.

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ISOLATED FRACTURES OF THE VERTEBRAL ARCH*†

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WHEREAS isolated fractures of the transverse process are apparently much more frequent than fractures of the vertebral body and the spinous process, and are described with increasing frequency, isolated fractures of the arch are quite rare. To facilitate their recognition it is necessary not only to observe gross deformities of the bone but also to look for fracture lines and changes due to fracture in the vicinity of the arch, a point which was emphasized by Reisner in 1931. It is necessary to differentiate fracture lines from appearances that in some cases may closely resemble fractures and which are not of traumatic origin.

The frequency with which fractures of the arch occur with compression fractures without an accompanying damage to the spinal cord is, to my mind, a foundation stone for the conception of Jaeger of the posterior aspect of the vertebral body as the pivotal point. Sternberg has pointed out the importance of its demonstration in differentiating post-traumatic from osteomyelitic wedge formation.

If we are to profit most from a study of these fracture lines in isolated fractures of the arch and also make a differential diagnosis of questionable findings in the vertebral body, we must pay more attention to localization of these conditions in the various segments of the vertebra, that is to say, whether they occur in the pedicle, the interarticular portion, the articular process or the lamina, and to investigate these points not only by the usual lateral and oblique projections from both sides but also by a roentgenogram to show the sagittal plane. As a definite point of orientation, the long ovals at the base of the arch are of great value. Since they are paired they are more useful as a point of orientation than the commonly used Köhler's "Tränenfigur."

Figure 1 illustrates the importance of the pedicle as a point of orientation. The patient was a woman, aged sixty, examined elsewhere on account of severe pain in the back, with negative findings. On the basis of the present

FIG. 1. Pedicle as point of orientation. Metastasis in the left pedicle of the seventh dorsal vertebra.

roentgenogram a diagnosis of osteoclastic metastasis to the left pedicle of the seventh dorsal vertebra was made; further examination of the skeleton showed similar areas in several ribs, and finally, as the most likely primary lesion, a left-sided hypernephroma was demonstrated. Paraplegia followed shortly, and death in six months.

This oval is exclusively the projection of the short bony cylinder of the pedicle which runs in a purely horizontal-sagittal direc-

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† Translated from the German by Eugene T. Leddy, M.D., Mayo Clinic, Rochester, Minnesota.

FIG. 2. Spondylolisthesis; fissure in the interarticular portion of the third lumbar vertebra.

tion. In the lateral view, this structure may appear as an oval open behind, a finding that increases its value as a point of orientation. Processes which are confined to the interarticular portion or to its process leave the oval intact; in other processes it is involved.

The interarticular portion is frequently shortened in the sagittal view. It is displaced downward at a greater or lesser angle from the pedicle, and runs at an angle of about 45 degrees to the sagittal plane. The posterior superior articular process approaches the anterior, and seems in the sagittal view less shortened. For this reason fracture lines can be easily recognized in this view because they do not overlap the vertebral body.

If we compare this with the "spondylolytic" changes in the last lumbar we are surprised to find, at least in those articles which I have read in the original, that nothing is said about the sagittal view. Certainly in cases of pure spondylolysis the vertebral body obscures this region, and the demonstration of a fissure is often impossible, especially when it runs more nearly in the frontal plane. This can easily be proved by means of an opaque band laid on a vertebra in such a way as to reproduce a fracture line in a macerated vertebra. The fissure in spondylolysis as viewed in the sagittal plane must run from within-upward-downward, and not involve the pedicle. If the opaque band is laid closely on the pedicle then it passes closely around the pedicle in the sagittal view. If it is applied between the transverse and superior articular processes, there is left free a triangular area lateral to the pedicle, whereas in the former case it was in close approximation to the pedicle. Let us now examine a case of spondylolisthesis:

In this case (Fig. 2), a man, aged fifty-one, the typical irregular fissure with sclerotic edges was found in the third lumbar with a slight slipping of the fourth lumbar as an additional finding. These changes in the lateral view suggested a saggital view (Fig. 3) which showed a break in contour irregularly running through the interarticular portion in a from within-upward-outward direction. On the left side, the break in contour did not go all the way through but on the external margin there was a deep narrowing between the superior and inferior

FIG. 3. Sagittal view of Figure 2. On the right there is complete separation of the interarticular portion, incomplete on the left.

articular processes. The vertebral body itself showed no traumatic changes.

Contrast with this a post-traumatic olisthesis* in a transverse fracture.

Figure 4 shows a completely intact body of the fourth lumbar displaced anteriorly on the fifth with narrowing of the fourth disc with a typical broad fissure through the interarticular portion. From this roentgenogram a diagnosis of spondylolisthesis was made. The sagittal view (Fig. 5) shows, on the other hand, displacement of the lower third transverse process to the right, broad break in continuity of the interarticular portion on the right, with displacement of the right upper articular process, decalcification of the pedicle and marked changes in the inferior articular process, a delicate irregular small fissure through the superior articular process and displacement of the spinous process to the left. On the left side, there is a more delicate but still detectable break of continuity through the interarticular portion with formation of an osteophyte which masks other detail. The pedicle is decalcified but still visible.

There was therefore an isolated fracture of the vertebral arch, a bilateral fracture through the interarticular portion on the right, with displacement of the pedicle and of the internal articular process and fissure of the superior articular process with dislocation of the spinous process but without any demonstrable fracture of the body of the vertebra.

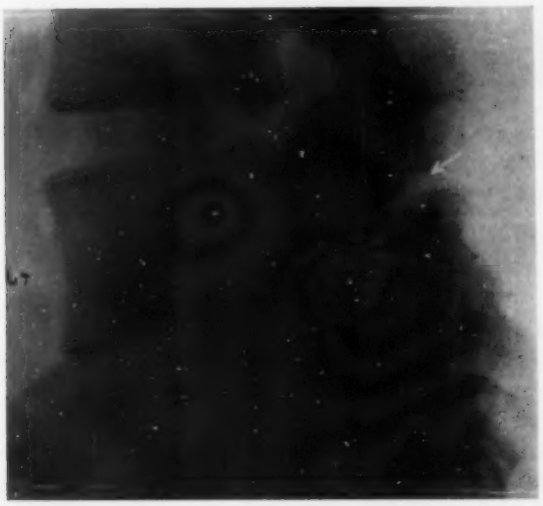

Fig. 4. Traumatic "olisthesis"; fissure in the interarticular portion of the fourth lumbar vertebra.

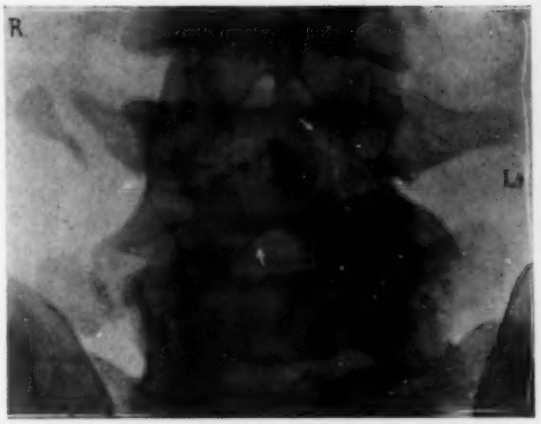

Fig. 5. Sagittal view of Figure 4. Fracture of the right interarticular portion with rotation of a bony fragment, sclerosing of the inferior articular process, fracture of the lamina and dislocation of the spinous process to the left.

The next case shows a regular but not completely penetrating slit in the right arch of the fifth lumbar (Fig. 6) and illustrates the difficulties of medicolegal judgments in cases of fissured arch.

It is surprising to see how well it is illustrated in the sagittal view. A fracture between the transverse and inferior articular processes cannot be shown. On the other hand, the fissure bends above the inferior articular process in a right angle but without completely passing through the superior articular process.

At first, the fissure might be regarded as nontraumatic because of its regularity and sharp outline. The lateral view showed a typical fracture of the superior surface of the fifth lumbar. Review of the sagittal view showed a great deal of irregularity in the spongiosa of the left interarticular portion and a fine, much smaller break in contour of a quite different appearance from that on the right, and decalcification and irregular outline of the inferior articular process of the fourth lumbar with deformity of the joint.

Diagnosis of fracture was at first disagreed in by the clinicians. Two years later neurologic ex-

* Properly: subluxation anteriorly. Jaeger correctly insists that the term "olisthesis" be reserved for those cases where trauma cannot be demonstrated, or those cases where gradual slipping has taken place, the etiology of which is still debated.

amination showed incontrovertible radicular findings and the neurologists asked for a myelographic examination. Now, strange to say, the fracture was overlooked again, and compensation was therefore denied the patient. The spine was then examined higher up. There were still some remnants of the contrast medium left and an old complete fracture of both articular surfaces of the first lumbar which I had missed on my previous more limited examination, and the fracture of the fifth lumbar was still demonstrable (Figs. 7 and 8).

or in other words, along the axis of the interarticular portion, may belong to this group. Reisner in 1931 described a fissure that ran sagittally through the interarticular portion and which involved the lamina, not an isolated fracture, it is true, but occurring with a compression fracture of the second lumbar; although it is not definitely mentioned there can be seen in the illustration an involvement of the pedicle. I regard the next case as an example of an

FIG. 6. Bone defect not going all the way through the right interarticular portion, an incidental finding in a case of fracture.

In spite of all this the slit-like transparent area which did not completely penetrate the right interarticular portion with a fracture of the roof of the fifth lumbar and the inferior articular process of the fourth is to be regarded as a partial spondylolytic bone defect. Reisner has described a more distinctly right-angled but smaller and longer defect of bone as congenital deformity of the superior articular surface of the body. If we consider slits perpendicular to the long axis of the interarticular portion and attempt to differentiate them from bone defects of non-traumatic origin, slit formation at an angle of 90 degrees to this, isolated fracture in the long axis of the arch.

A moderate-sized vigorous man was examined several months after a fall on the buttock. In the anteroposterior view, that is perpendicular to the course of spondylolytic slits, the left arch of the fifth lumbar (Fig. 9) was penetrated by a sharply demarcated line running from the inferior articular process through the interarticular portion as far as the pedicle and through its lower third. The slit showed, where it changed its course, a short, stepped angulation. At its posterior end it involved the compacta of the root of the arch to a slight extent. In addition to a slight sclerosing of the margins we found the lateral superior contour

of the pedicle to be irregular, the lower part of the superior articular process more transparent. From this point a delicate irregular jagged slit (which does not show up well in Figure 9) ran into the left transverse process. The vertebral body of the fifth, which was sacralized, and the other lumbar vertebrae showed no signs of fracture. There was a slight dipping to the left of the superior articular surface of the body of the fifth lumbar.

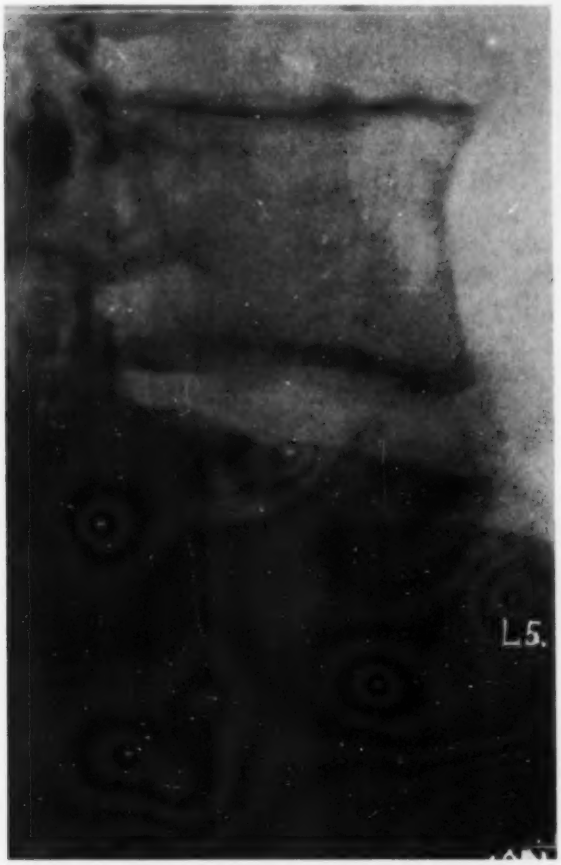

Fig. 7. Frontal view of Figure 6. Fracture of the superior surface of the fifth lumbar. Residue of a previous myelography.

On the basis of the course, the dehiscence of the compacta and the fissure through the transverse process and decalcification of the superior articular process a diagnosis of isolated fracture of the left fifth arch seems correct.

A similar case was sent to me in consultation following an accident.

A railway employee, aged forty-one, two years previously had fallen on the ice hitting the lumbar region. He arose with difficulty but was able to walk home. He took hot baths with some relief. Since then he had had pain in the sacral region and could not stand comfortably for any length of time. Roentgen examination had been negative.

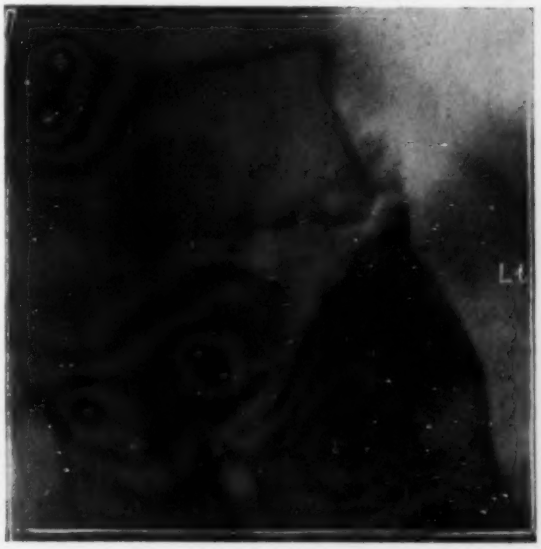

Fig. 8. First lumbar of the same case as Figures 6 and 7. Vertebral body completely fractured.

The sagittal view, left (Fig. 10) shows an irregular jagged slit in the fifth lumbar going from the posterior superior articular process through the interarticular portion to the superior articular process where the fissure was lost to sight because of its lateral course. In comparison with the right side the pedicle was less

Fig. 9. Fracture line of the fifth lumbar vertebra involving the long axis of the arch to the pedicle.

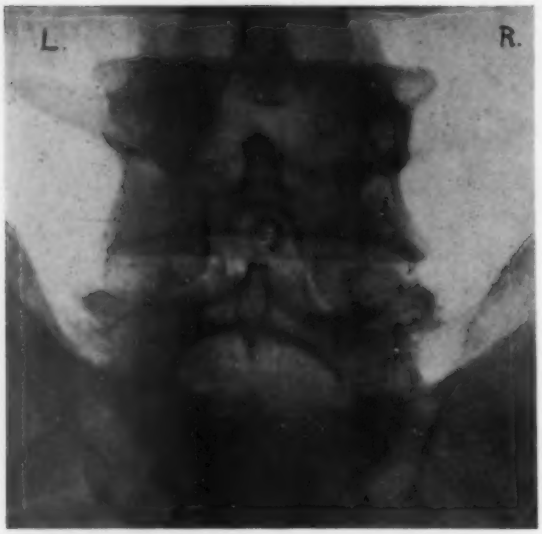

Fig. 10. Fracture in the long axis of the arch, decalcification of the superior articular process and of the pedicle.

calcified and more indistinct. The left superior articular process was rotated frontally (apparently broadened), of irregular structure and more decalcified. Also the left inferior articular process of the fourth lumbar was decalcified to some extent, but had a regular outline. In the region of the superior articular process there was marked sclerosis around the fissure, and at the posterior end of the fissure the compacta was irregular. The whole superior articular process on the left was more vertical than the right, even when the projection was absolutely symmetrical. The lumbosacral joint on the left was sclerosed and not very distinct, while on the right the ends of the joint were quite plain. The bodies of the lumbar vertebrae as shown also on lateral view were completely intact, but the region of the nucleus of the fourth intervertebral disc showed some delicate loss of calcium (very likely post-traumatic).

Therefore this is a case of isolated fracture in the long axis of the fifth vertebral arch involving at the same time the regions of the upper and lower joint surfaces. The fracture line is narrower than in Figure 9, but around it there is more marked sclerosis. The symptoms are referable to the fracture, which, it is true, was not a bad one. Considering the negative neurologic findings, disability should be rated at 20 per cent at most.

Both cases showed fracture fissures. From the configuration alone it is impossible to draw any definite conclusions about the nature of the fissure formation; the course of the fissure also makes the possibility of some congenital defect quite unlikely. As evidence for the traumatic nature of the defect, there are the displacement of the compacta at the posterior end and the irregularity of the same structure, just as in the second case there were irregularity of the sclerosis and deformity of the arch; finally, the involvement of the pedicle, the fissure passing into the transverse process in the first case, and in the second the decalcification of the superior articular process. In this kind of gaping fractures of the arch, Reisner points out that the intact supportive structure of the individual vertebrae holds the spine together so that no dislocation follows. In the first of the two cases (Fig. 9), even though the fracture was confined to one arch, there was a deviation of the axis toward the side of the fracture. In another case also (Fig. 5), a fracture with several fissures but which was confined to the arch of a single vertebra produced moderate displacement. How far the supporting structures of the spine may remain intact in such isolated fractures of the arch is still an open question.

In cases of fracture around the articular process, the supporting structures, at least in the immediate vicinity of the joint, must be damaged to some extent. Reisner is right in stating that these isolated arch fractures are not to be counted as severe injuries provided there is no gross dislocation. This statement is especially true in cases of isolated fractures of a single articular process.

I have frequently found involvement of the superior articular process in cases of isolated fractures of the arch, even when they are unilateral, as Figure 10 illustrates. Böhler and Heuritsch reported a case of bilateral fracture of the superior articular process, but on the basis of a bilateral fracture through the interarticular por-

tion it is a traumatic "olisthesis" with an almost horizontal fracture line. The pedicle on both sides is "lengthened" in the vertical direction, its contours broken at the site of the fracture; evidence that the fracture continued into the pedicle; this all points to the fact, to judge by the sketch they presented, that the fracture, at least on the one side, extended horizontally into the transverse process. Also Schinz pointed out in his case of rupture of both upper processes (Fig. 1056 in his textbook) the break in the oval in the sagittal view as a fracture of the pedicle; the transverse process in question had been torn off (not olisthesis). Kienböck and Brausewetter have recently reported an isolated fracture of an upper articular process in the sagittal view. In this case the pedicle was uninvolved.

The next case is a fracture at the root of the superior articular process demonstrated by frontal projection (Fig. 11) as a secondary in a compression fracture with slight dorsal subluxation of the vertebra above (with extensive rupture of the Lig. long. ant. and of the Lig. supraspinale D12 to L1) because fractures of the articular process in this view are often very difficult to demonstrate. This is easier to do by an oblique projection, but this may produce many confusing details. The sagittal view showed marked changes in the structure in the body and arch of the first lumbar with a horizontal fissure not going all the way through the left interarticular portion of the first lumbar, arthrotic changes in the small joints between the first and second lumbar, but the fissure could not be demonstrated in the superior articular process of the second lumbar. This is explainable by the steep course of the fracture line in lateral view. The pedicle on the left side was not involved, on the right its margins were irregularly broadened, the articular process was thickened and deformed, so that the fracture must have involved the right superior articular process as far as the pedicle.

In my material I have no case of isolated fracture of a superior articular process.

In cases of fracture around the inferior articular process, one must be very careful in making the diagnosis of fracture. Ren-

Fig. 11. Fracture line in the superior articular process of the second lumbar vertebra with a compression fracture of the first lumbar.

dich and Westing in 1933 described 6 cases of fissure in the inferior articular process as due to accessory bone nuclei occurring at ages from nineteen to sixty-seven, and this condition was bilateral in 2 cases. Fulton and Kalbfleisch reported 2 cases of fissure in the lower articular process which were due to congenital anomalies.

For comparison Figure 12 shows a nontraumatic unilateral defect running diagonally across the inferior articular process of the fifth lumbar.

The patient was a boy, aged eighteen, who had severe pain in his lower back. No antecedent trauma. The regular wave-shaped defect was sharply outlined, the surrounding parts had normal calcification and normal structure. It had the same appearance as an epiphyseal joint.

The origin of these "fissures" has not been completely investigated, at least not from the same point of view. The conception of zones of reconstruction (Umbauzonen) will be a step in progress if we can determine the conditions which may lead to their formation. Whether the ossification of the arch proceeds from several centers and remains incomplete or whether there are accessory bone nuclei which have

Fig. 12. Congenital bone defect of an inferior articular process. Incomplete union of the first sacral arch. Deformity and thickening of the articular process of the sacrum on the other side.

not united with the main nucleus, it seems that the conditions in each case indicate a congenital origin. Opposing this view is the fact that the students of pathologic anatomy do not agree about the ossification of the arch.

If one can imagine that such a congenital defect involved the whole interarticular portion one can easily imagine that with the forces pulling and pushing at this point in the lower lumbar spine a defective interarticular portion would result, especially if the fissure is bilateral, and that even if the supporting mechanism is intact, in the course of years a spondylolisthesis might result.

Figure 13 illustrates one of these isolated areas of decreased density in an articular process which resemble zones of reconstruction (Umbauzonen).

Injured a week previously, a patient complained of pains in the sacral region. The lower lumbar bodies were normal. A broad irregular fissure in the fifth lumbar was seen in the sagittal view to curve through the base of the left lower articular process, separating it from the spinous and transverse processes. The surrounding parts were sclerosed over a wide area. There was thickening and deformity of the articular process of the sacrum, less marked changes were seen in the other joints of the fifth lumbar. The tendency was first to think of a zone of repair, discounting the fact that the right transverse process was fractured and the right pedicle was slightly deficient in calcium: therefore an isolated fracture of the left lower articular process which continued into the interarticular portion between the superior and transverse articular process. Apparently also the lower tip of the left lower articular process of the fourth lumbar is fractured. But this optical illusion is caused by the overlapping edges of the fourth lumbar which may be mistaken for a fracture line.

This fracture must be due to some previous injury, for it is unlikely that such extensive reaction of bone could take place in less than a week. Therefore the changes could have no relationship to the recent trauma.

SUMMARY

Isolated fractures of the arch, particularly in the lumbar spine, may result from mild trauma. They explain the cause of obscure pains in the sacral region, they are easily missed if the involved portion of the arch is not carefully studied. Their importance in accident suits is emphasized, and their exact localization in the fissure in the pedicle, the interarticular portion or the superior articular process is discussed with special reference to the importance of the sagittal view (1) with reference to a trau-

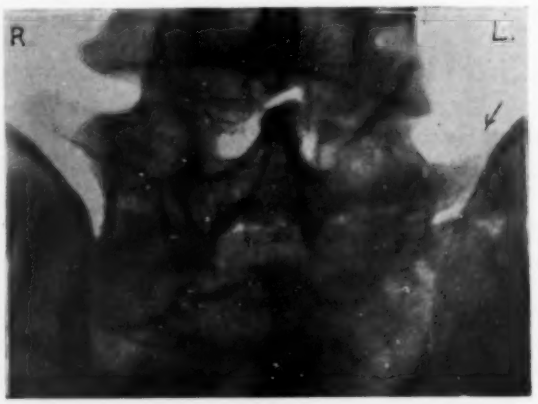

Fig. 13. Fracture line of an inferior articular process through the interarticular portion and the transverse process. Rupture of the tip of the transverse process.

matic "olisthesis" with bilateral fracture of the interarticular portion and the right articular process; (2) two cases of unilateral fracture along the long axis of the arch extending from the posterior margin of the articular process to the pedicle; (3) an isolated oblique fracture of an inferior articular process which extended through the interarticular portion to the transverse process. The fracture line in a superior articular process is presented. Isolated fractures and congenital defects seem to be much less frequent in the superior process.

These fractures are contrasted with (1) a true olisthesis, the fissure of which in the sagittal view could not be differentiated from a fracture; (2) from a congenital unilateral "spondylolysis" which did not pass completely through the interarticular portion as a secondary finding in a case of fracture of that vertebra and of some above it; (3) from a congenital fissure-like defect in an inferior articular process. In the question of non-traumatic fissure formation the conception of zones of reconstruction (Umbauzonen) for the time being should be entertained with great reservation.

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ROENTGEN DIAGNOSIS OF OSTEOMYELITIS OF THE VERTEBRAE

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THE chief purpose of this discussion is to consider the pyogenic type of osteomyelitis of the spine with special reference to the roentgenographic findings.

Early reports of osteomyelitis of the vertebrae were made by Valleix[9] in 1835 and by Stanley in 1849. No comprehensive articles, however, appeared until the reports of Lannelongue[5] in 1880, and Hahn[2] in 1895 and 1899. Out of a total of 661 cases of osteomyelitis, involving all of the bones, Hahn found 51 cases in small and irregular bones, and, out of these 51, only one case involving the vertebrae. In 1896 Makins and Abbott[3] made an important contribution to the literature, which was followed in 1906 by an excellent review by Donati.[1] Donati collected 55 cases from the literature and added one case of his own. Many other case reports followed, and in 1915 Volkmann[10] collected 83 cases from the literature and added 4 of his own. Volkmann discussed in a scientific manner the symptoms, pathology, diagnosis, and treatment as it existed at that time.

The use of the roentgen ray has aided greatly in the diagnosis. It has probably been the greatest single advancement in the diagnostic procedure of this condition in recent years. Prior to its use, the diagnosis was frequently more difficult and often remained uncertain until confirmed by surgical intervention or by necropsy.

The disease may manifest itself in the acute or chronic form. The acute form is associated with high temperature, severe pain, marked prostration; oftentimes associated with paralysis, involvement of the spinal cord and a high mortality. This is the form that is most commonly described in the literature.

In our series of 5 cases, 3 were of this type. The roentgen findings differ somewhat from the chronic type. All 3 acute cases had definite roentgen findings at the first examination made soon after the onset of the initial symptoms.

The chronic form is milder in all its aspects. It probably occurs as frequently as the acute form.

Alan DeForest Smith[6] has published an excellent article on the benign form in which he reported finding the benign type more frequent than the acute fulminating type in a series of 17 cases.

Steindler[7] has reported 12 cases, 6 acute and 6 chronic in the original onset, though all were observed in the chronic stage.

Sussman[8] presents 4 cases and describes the roentgenographic observations made during the course of the disease.

The age incidence in a series of 59 cases reported by Volkmann was as follows: 18 in the first decade; 31 during the second; 7 during the third; 1 in the fourth, and 2 during the fifth. The affection is more frequently seen in males than in females. In Volkmann's series 72 per cent were males.

The organism is, in the vast majority of cases, the *Staphylococcus aureus*. In this discussion, as stated above, we are considering only the pyogenic type of infection, and have not included other conditions such as typhoid, paratyphoid, or luetic involvement, except in the differential diagnosis. Seth Selig has reported a case of *Bacillus proteus* infection of the spine. In a large number of cases it is a metastatic infection from some discoverable source, such as a boil, carbuncle, or an abscess located in some other part of the body. It may also occur by direct extension of an infection. The question of trauma as a factor in the etiology may at times have a legal bearing in accident or compensation cases. Trauma may produce a point of lowered resistance where thrombosis may occur and prepare the site for

lodgment and multiplication of bacteria. Steindler states that in one of his cases trauma was a definite factor in the history, and that osteomyelitis of the spine followed one month later.

The occurrence of osteomyelitis of the vertebrae is probably more common than statistics would indicate. The real nature of the disease is often not recognized. The severity of the symptoms may lead to an erroneous diagnosis such as myelitis, retropharyngeal, paranephritic, retroperitoneal, or pelvic abscess, and the underlying bone lesion remain unrecognized. On the other hand, the mildness of the symptoms of the low grade and chronic form may not attract sufficient attention to the vertebrae, and the true condition be entirely overlooked. The patient may be confined to bed from some obvious infection in some other part of the body, and when the pain is complained of in the spine it may be considered as a part of the general toxic condition, and thus escape a correct diagnosis.

The value of the roentgenogram in many of these cases can scarcely be overestimated. Early in the disease the roentgenogram may be negative or it may show only a slight haziness or indistinct changes in the bony structures. Osteomyelitis of the spine develops as a subperiosteal type, or, in the young individual, as an epiphyseal separation. The tendency to new bone formation is characteristic of this condition, and the lesion may first be noted on the roentgenogram as a rarefying and proliferative osteitis. More commonly it develops as a destructive bone lesion, which shows early new bone formation. The outlines of a paravertebral abscess may be present early. It is not, however, a constant finding. The intervertebral disc may or may not be involved, although a uniform narrowing is frequently seen. The tendency to form new bone may prevent deformity such as kyphosis or scoliosis. In chronic benign cases, where pain is not severe, marked deformity may take place before the patient comes under observation. In the benign form the destructive bone lesion may be less clearly visualized owing to the tendency to form new bone.

The infection may involve the body or any part of the neural arch without involving the body, or the entire vertebra may be involved. The disease may be limted to only one vertebra, or it may involve several adjacent vertebrae, or there may be intervening normal vertebrae.

Any portion of the vertebral column may be affected, but most of the cases are in the lumbar region, next, the cervical, dorsal and sacral. Mathieu[4] puts the order of frequency as lumbar, dorsal, cervical, and sacral, and says that the posterior arches are more often involved than the body except in the cervical region.

It is necessary to have a maximum of detail on the roentgenogram. It is our custom, routinely, to make the anteroposterior films stereoscopic. This gives a better opportunity to study the laminae and articular processes. If the examination is to include the lumbar vertebrae, and there are no contraindications, the patient is prepared by giving a laxative in the evening preceding the examination and no breakfast until after the films are taken the following morning.

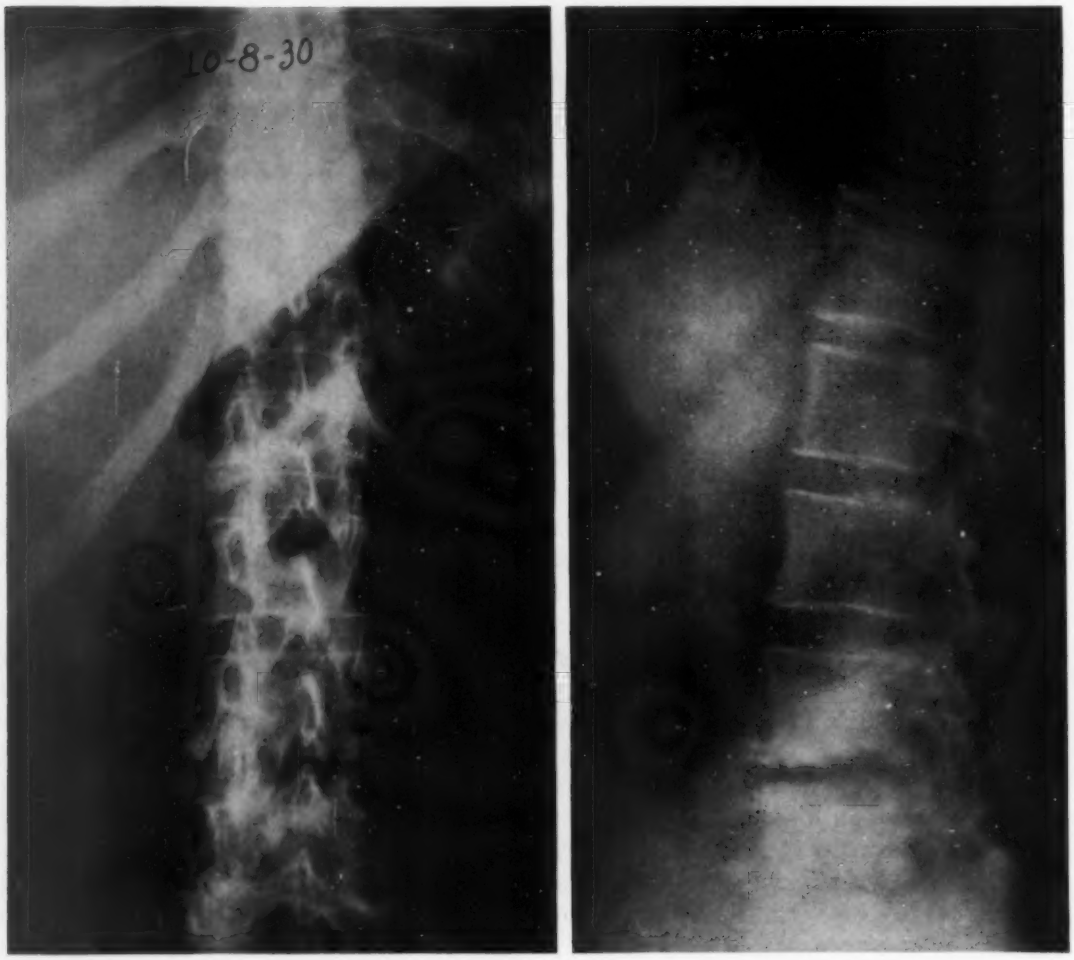
The differential diagnosis from tuberculosis may be difficult. The intervertebral cartilage is usually not involved to the extent seen in tuberculosis. There is more apparent destruction of the vertebrae in many cases with less deformity. There is less tendency to form new bone in tuberculosis. Successive roentgenograms taken during the course of the disease may be necessary in the differential diagnosis. Typhoid osteomyelitis simulates tuberculosis rather than pyogenic osteomyelitis. In fact, it may have all the characteristics of tuberculosis except the clinical history. It is, however, usually more rapid in onset.

Metastatic cancer, especially the combined osteoclastic and osteoblastic form, is also at times difficult of differentiation.

Luetic involvement of the spine or pressure necrosis may at times give appear-

ances similar to pyogenic osteomyelitis. The serological and clinical findings will aid in the differentiation. In case of pressure necrosis it may be possible to demonstrate roentgenologically the source of the pressure.

Actinomycosis of the spine usually involves two or more vertebrae; areas of rarefaction are clearly defined and often interspersed by apparently normal bone texture. The bodies, pedicles, and laminae are usually involved, and the adjacent portion of the ribs. In spite of the rather extensive amount of destruction in the bodies of the vertebrae, there is very little tendency to collapse and deformity. Roentgen examination of the lungs may show the involvement and the organism may be demonstrated in the sputum or in a draining sinus.



A *B*

FIG. 1. Case 1. *A*, anteroposterior view, and *B*, lateral view of lumbar vertebrae taken on October 8, 1930. Note the destructive bone lesion (osteomyelitis) with new bone formation involving the third, fourth, and fifth lumbar vertebrae.

Two typical case histories follow.

REPORT OF CASES

CASE 1. Patient of Dr. Wm. G. Strobel. Female, aged sixty, white, married. Referred to me for roentgen examination on October 8, 1930. Her chief complaint was severe pain in the lower part of the back. The pain was constant, sharp in character, and exaggerated by

movement. It did not radiate beyond the lumbar area.

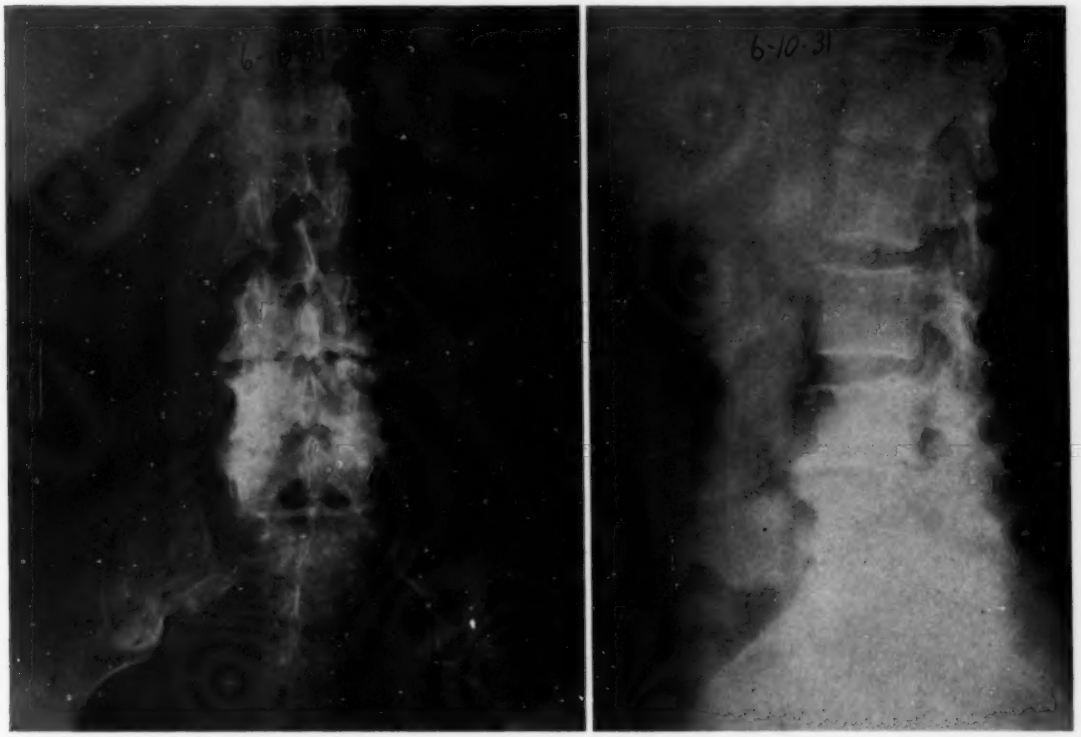
Past History. Patient gives history of having had attacks of pain in right upper quadrant of abdomen. This pain did not radiate and was not followed by jaundice. The attacks have been accompanied by much gas in the stomach. Fatty foods were not well tolerated.

The family history was essentially negative. There was no history of tuberculosis.

Examination revealed a well-developed and obese patient. There was slight tenderness and rigidity in the right upper quadrant. The urine was negative except for a faint trace of albumin and a few leukocytes per high power field. The hemoglobin was 76 per cent, red blood cells 3,880,000, white blood cells 11,400. The temperature was only slightly elevated except on a few occasions when it was moderately high.

Roentgen examination of the gallbladder and stomach revealed a non-functioning gallbladder, and a mass, probably inflammatory, which was producing a deformity of the duodenum and about 60 per cent retention of the barium meal in six hours.

Roentgen examination of the lumbar vertebrae made on October 8, 1930 (Fig. 1, *A* and *B*) revealed a destructive osteomyelitis of the third, fourth, and fifth lumbar vertebrae with beginning new bone formation. The intervertebral disc between the third and fourth vertebrae is fairly well preserved, but the disc between the fourth and fifth vertebrae is destroyed.



A *B*

Fig. 2. Case 1. *A*, anteroposterior view, and *B*, lateral view of lumbar vertebrae taken on June 10, 1931, show marked healing with new bone formation and beginning ankylosis. This patient has remained well since.

At operation a large parahepatic abscess was found surrounding the gallbladder and duodenum. Drainage was established. No gallstones were found, and no attempt was made to remove the gallbladder. The patient made a good recovery after a rather stormy convalescence.

The spine was treated conservatively and has done very well. The patient is living and well at the present time, and is free from symptoms.

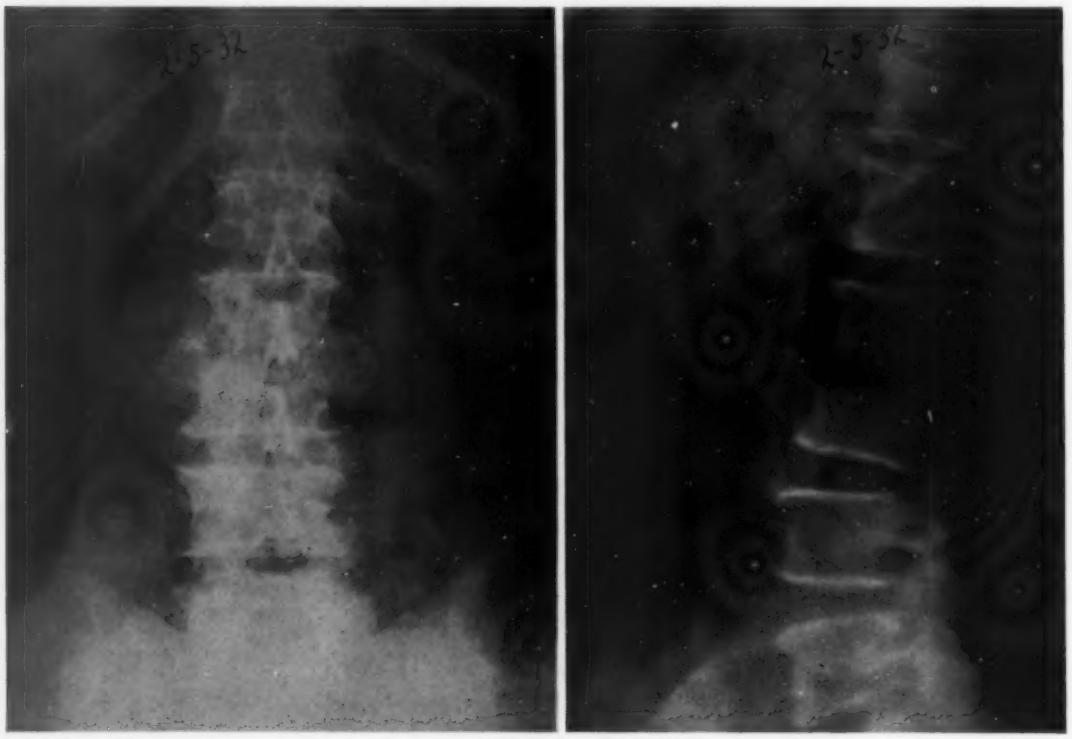
Follow-up films were made of the lumbar spine on June 10, 1931 (Fig. 2, *A* and *B*) which

show a marked amount of new bone formation with beginning ankylosis of the involved vertebrae. The intervertebral discs have been largely destroyed.

Case II. Patient of Drs. William R. Bagley and Elizabeth C. Bagley. Female, aged sixty-eight, white, married. Referred to me for roentgen examination February 4, 1932. She gave a history of pain in the lumbar region for eight or nine weeks. The pain was excruciating and increased by any attempt to move, although there were spasms of pain not associated with motion. The pain did not radiate to any other part of the body.

Past History. She has had pain in the right hip joint for many years, and has not felt well for some time. No cough, and no digestive disturbances. There was no uterine hemorrhage or discharge, although a tumor (known to the patient) has been present in the lower abdomen for some time.

The examination, as recorded by the attending physicians, revealed a well-nourished, but somewhat dehydrated patient. The examination was difficult because of severe pain, which was not relieved by one-fourth grain of morphine sulphate. Her temperature was only slightly or moderately elevated; the red blood count was 4,016,000, white blood count 29,700, polymorphonuclears 87 per cent, lymphocytes 12 per cent, eosinophiles 1 per cent. Repeated Wassermann tests were negative. The urine was negative except for a trace of albumin. There was a large smooth tumor in the pelvis, extending up almost to the umbilicus.



A *B*

Fig. 3. Case II. *A*, anteroposterior view, and *B*, lateral view of lumbar vertebrae taken on February 5, 1932, showing destructive lesion of second and third lumbar vertebrae with beginning new bone formation.

Stereoscopic roentgenograms of the pelvis were taken. They showed a large calcified area in the lower abdomen on the right side, which was interpreted as a calcified fibroid tumor or an ovarian cyst. The right hip joint showed an old infectious arthritis. A roentgenogram of the chest was negative except for calcification of the arch of the aorta and a dilatation of the descending portion of the aorta. The roentgen examination of the lumbar vertebrae (Fig. 3,

A and *B*) showed a destructive lesion of the adjacent portions of the second and third lumbar vertebrae. There was evidence at this time of beginning new bone formation. and the disc was partially destroyed, with some angulation of the vertebrae at this point. The differential diagnosis at this time rested chiefly between a pyogenic infection, tuberculosis, and a Charcot joint.

A laparotomy was done on February 15, 1932, and a large and partially calcified cyst of the right ovary was removed. The gallbladder was distended and full of calculi and was also removed. The lesion in the spine was palpable, although there was no paravertebral abscess.

Following the operation the patient did very well for a number of weeks. The pain in the back became much less. She was able to move about in bed quite easily. Further roentgenograms were taken of the lumbar spine on March 14, 1932 (Fig. 4, *A* and *B*) for comparison with the previous films. Nature's effort toward reconstruction and repair in an attempt to stay the disease is quite evident on these films. The diagnosis is also more definitely established as a pyogenic osteomyelitis.

A few weeks later she developed a severe pain in the substernal region, which was followed by difficulty in swallowing. Roentgen examination of the chest and esophagus on April 8, 1932, revealed a definite increase in the size of the descending aorta previously reported on the examination made two months previous. There was evidence at this time to indicate a rupture of the aneurysm with free fluid in the mediastinal space, which was producing pressure on the esophagus sufficient to cause definite retention of food in the upper part of the esophagus.

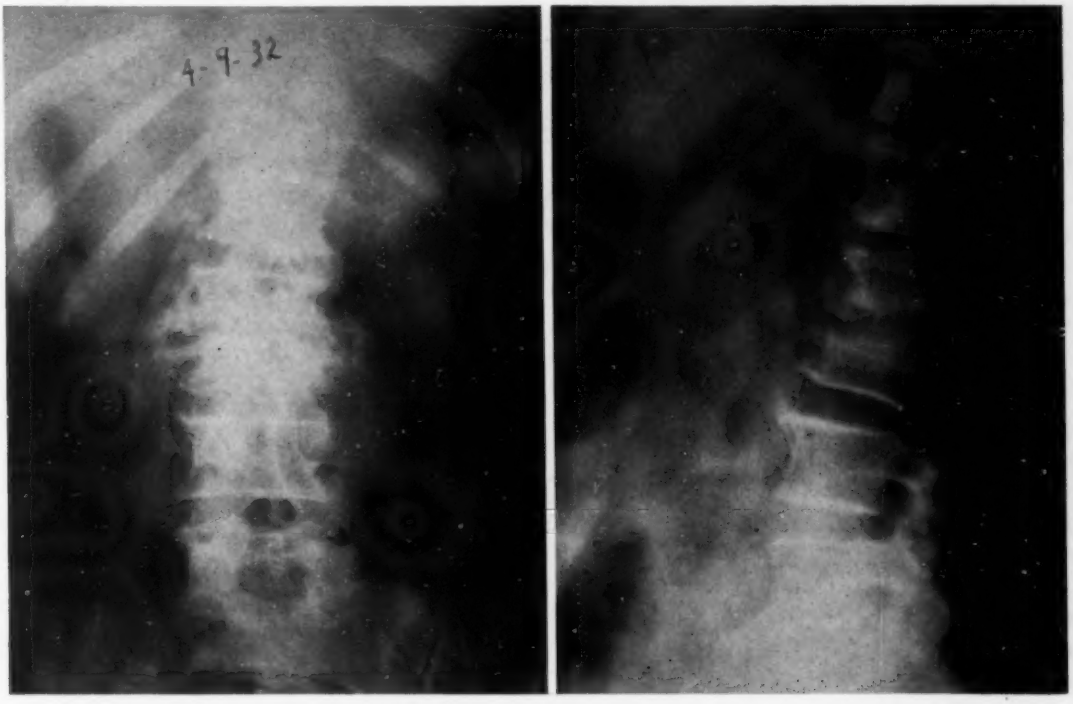


Fig. 4. Case 11. *A*, anteroposterior view made on April 9, 1932, and *B*, lateral view made on March 14, 1932, of the lumbar vertebrae. Post-mortem examination made on April 11, 1932, revealed a pyogenic osteomyelitis of the vertebrae.

On April 11, 1932, the patient died. An autopsy was done by Dr. George Berdez, pathologist at St. Mary's Hospital, which revealed a ruptured aneurysm of the descending aorta. The ascending aorta was slightly dilated and had areas of calcification. Microscopic examination of the aorta near the aneurysmal sac showed marked arteriosclerotic changes. There were no lesions suggesting a luetic involvement.

There was no evidence of tuberculosis in the lungs or in any other part of the body.

The spinal lesion was a pyogenic involvement. Sections through the spinal cord were negative.

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THE SUBMENTOVERTEX VIEW AS AN AID IN MASTOID ROENTGENOGRAPHY*

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UNTIL a few years ago the roentgen examination of the mastoids consisted in the production and interpretation of a lateral oblique view of the two mastoids. This projection is usually referred to as the Law position. Since clinical writers emphasized the important rôle the petrous portions may play in the course of mastoid disease, many roentgenologists have been adding the demonstration of the petrous portions as a matter of routine. A number of different projections are available for such a procedure. In selecting a standard technique, I had to consider the particular needs existing in a communicable diseases hospital. Here the majority of patients are infants and children, frequently severely sick from acute illness, and the difficulties are increased by the fact that the roentgen technician is not allowed to touch the patients personally.

Under these circumstances, a technique portraying both petrous portions simultaneously is to be preferred to one requiring individual exposures for the two petrous portions. Among the exposures resulting in a simultaneous demonstration of both petrous portions the submentovertex projection, also called inferosuperior projection and base plate, is the one to be recommended. This projection combines simplicity and speed with a sufficient amount of accurate information. It requires but an ordinary amount of care and little manipulation to bring the patient's head into the desired position and to adjust it truly symmetrically. As a rule, all but the most unmanageable patients remain motionless in this not uncomfortable position. In our particular situation this technique works much more satisfactorily than any of the other methods available.

If a large enough cone is used, the film, in addition to the petrous portions, shows symmetrical projections of the two mastoids. A great part of our mastoid interpretation is based on a comparison of the shadow density of the two mastoids, and a *simultaneous symmetrical demonstration of the two mastoids on one film* offers an ideal opportunity to compare shadow densities, as the roentgenographic factors on either side are perfectly identical. Whereas the conventional lateral oblique views are unsurpassed in the demonstration of detail, the simultaneous symmetrical projection of the two mastoids on one film is better suited for comparing densities. Such a projection has the additional advantage of avoiding superimposition of the mastoid and its soft tissue coverings. Particularly when these tissues are swollen, which happens so often, either as a consequence of mastoid disease or as an independent affection, they seriously interfere with the comparability of the two Law projections.

Since it became our custom to add a base plate to the mastoid routine, more than 350 mastoid examinations have been performed. It is indeed striking to observe the pronounced differences of opacity that may occur in the two mastoid areas of the base plate. No doubt, every examiner must be impressed by the ease with which the difference of illumination can be determined on the base plate. In a considerable percentage, the difference of opacity is decidedly more marked on the base plate than on the Law projections. The question arises how much reliance can actually be placed on such a finding. I was unable to obtain the answer to this question from the available literature.

A study of the literature reveals that a number of authors emphasize the desirability of examining the mastoid by more

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than one view. Some recommend a simultaneous symmetrical demonstration of both mastoids on one film. I wish to cite two instances only: Law[1] himself now adds to his standard views a vertex-mental view for the petrous pyramids and a 23° angle posteroanterior view for comparing both mastoids. Worms and Bretton[2] recommend adding to the unilateral exposures the base plate and still more emphatically the fronto-suboccipital view as a means of comparatively judging the transparency. But none of the writers seems to have investigated the degree of dependence that can be placed on the findings so recorded.

Therefore, I undertook the task of correlating the mastoid findings on the base plate with whatever actual facts were known about the case. The study was based on a series of 73 unselected consecutive cases that had been roentgenographed and subsequently operated upon. I reviewed the two mastoids on the base plates of these patients, bearing in mind in each case the history, the clinical, otological, and laboratory data, the roentgen signs seen on the conventional lateral views, the preoperative course, the operative findings, and the postoperative course.

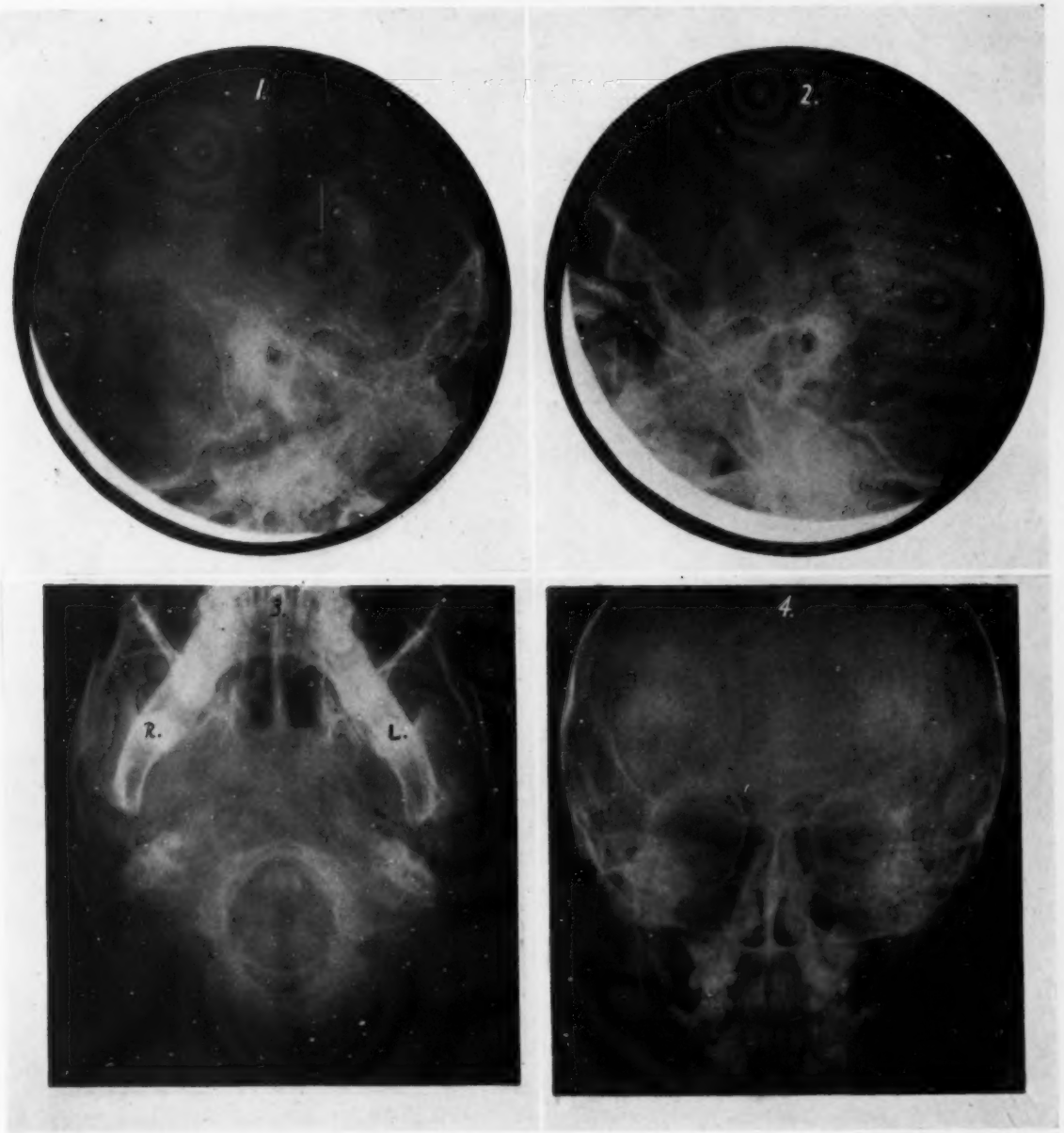
The result of these studies is as follows: In 61 of the 73 cases, the presence of increased mastoid opacity on the base plate was in complete harmony with the remainder of the findings. The base plate might have conveniently served to support the diagnostic opinion formed on the strength of the conventional views. In 14 out of these 61 cases, the base plate might have been of deciding value. This applies chiefly to cases of diploic character or of insufficient cell development. The conventional views showed nothing but slight differences of opacity, whereas the base plate revealed the differences more markedly and, therefore, might have been decidedly instrumental in bringing about diagnostic conclusions. In cases where both sides are involved, the base plate, as a rule, demonstrates bilateral affection and may often help to determine the side more intensely affected. Another class of cases deserves special mention: the abundantly pneumatized mastoids, where just one portion of the mastoid is affected. Here the illumination of the unaffected cells within the involved mastoid tends to diminish the difference of opacity which exists between the two mastoids. But the base plate may definitely point the way to proper interpretation.

In 10 of the 73 cases, the changes on the base plate were in accord with the actual pathology as established by operation, etc. But, in these instances, the help to be derived from the base plate had to be classified as indifferent, as far as the mastoid study was concerned. In these 10 cases, the base plate could have easily been dispensed with, had it not been for the sake of the petrous portions.

In the remaining 2 cases of the whole series of 73, the base plate—should it have been used exclusively, that means, without the standard lateral oblique views—would have been misleading. Both these cases were instances of bilateral affection. It so happened that the side more intensely affected showed less opacity than the better side. The explanation is simple enough. The inflammatory exudate plus bone on the better side casts a denser shadow than the exudate alone after the disappearance of the necrotic bone on the worse side. In both cases, the roentgenologist actually was not misled, as the very obvious findings on the conventional views were unmistakable and as the knowledge of the history, clinical, and otological data had put the roentgenologist on his guard. Such knowledge, we all admit, always has been and probably always will be indispensable to the roentgenologist; particularly in the event of bilateral involvement. Yet, as mentioned before, in the majority of cases of bilateral affection, the base plate might have been of unquestionable assistance.

[1] Law, F. M. Roentgen examination of the mastoid processes. AM. J. ROENTGENOL. & RAD. THERAPY, 1934, *31*, 482–486.

[2] Worms, G., and Bretton, R. L'exploration radiologique du massif pétro-mastoïdien. *J. de radiol. et d'électrol.*, 1929, *13*, 23–37.

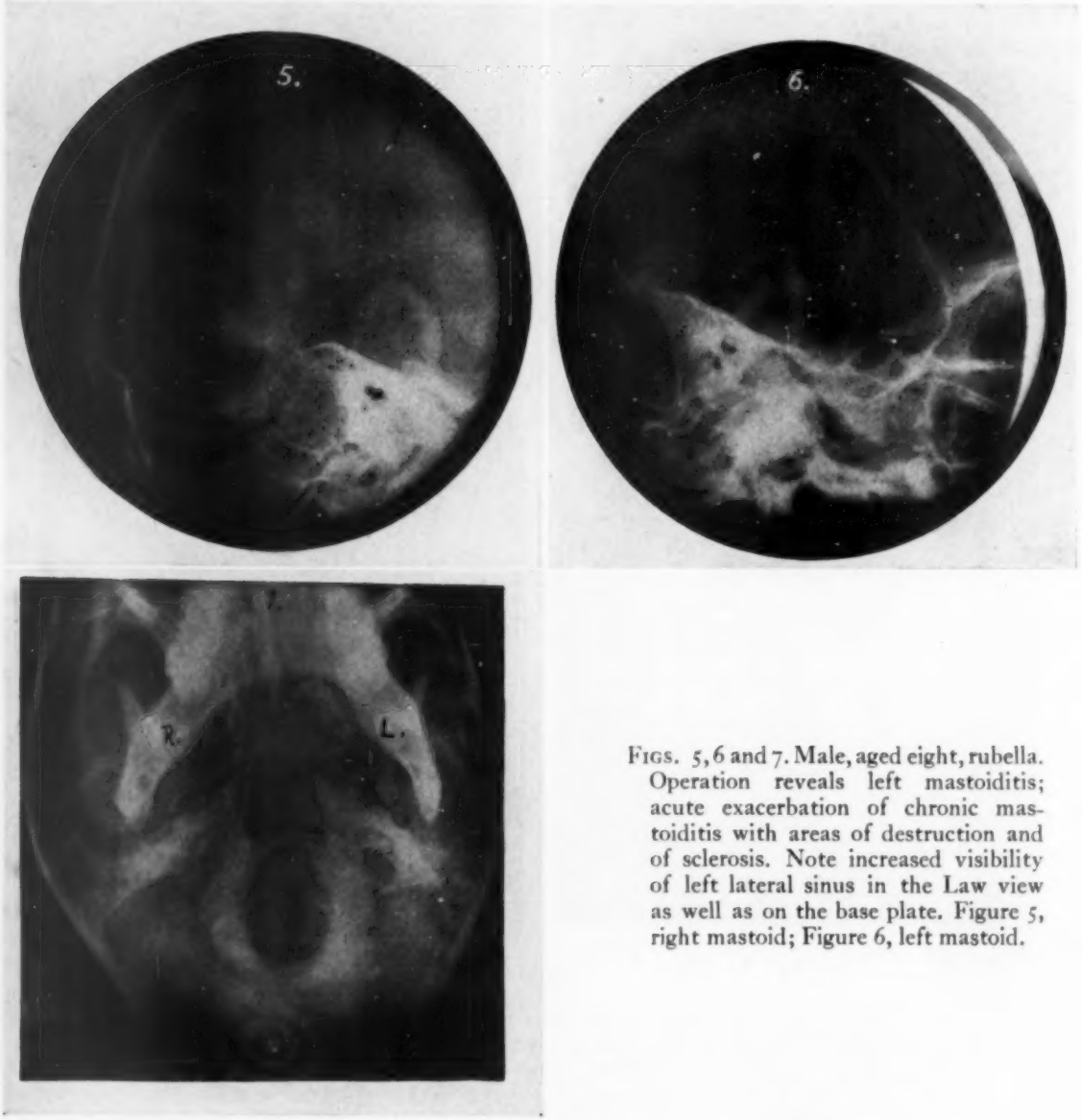


Figs. 1, 2, 3 and 4. Male, aged eight and a half, scarlet fever. Right destructive mastoiditis, confirmed by operation. Note evidence of mastoid affection on the base and posteroanterior plates. Note demineralization of tip of petrous pyramid on the base plate. Figure 1, right mastoid; Figure 2, left mastoid.

As a whole, this investigation justifies the conclusion that the base plate, besides demonstrating the petrous portions, is a very dependable and a very valuable aid in the study of mastoid affection proper. It can never replace the conventional mastoid views, but, in the hands of the critical interpreter, it can serve as a convenient and reliable supplement to the findings obtained from the conventional lateral oblique views. In cases of bilateral affection, the interpreter has to be particularly alert and has to direct double attention to the history and the otological findings.

So far, I have been discussing nothing but differences of shadow density as they

manifest themselves on the base plate. In a number of cases, one can see, in addition to shadow differences, a condition that warrants description. This is a cherry-sized, well-defined circular or elliptical area of increased illumination, adjacent to the inner aspect of the posterior portion of the petrous pyramid. Every one of these cases was affected by severe mastoiditis. I think we are dealing with a phenomenon corresponding to the sign of increased visibility of the lateral sinus, so familiar to the reader of mastoid films in the Law position. What we see on the base plate of these cases is an abnormal prominence of the end of the lateral sinus, due to affection of the adjacent bone. Thus far I have had no chance to check this conjecture by an autopsy.



FIGS. 5, 6 and 7. Male, aged eight, rubella. Operation reveals left mastoiditis; acute exacerbation of chronic mastoiditis with areas of destruction and of sclerosis. Note increased visibility of left lateral sinus in the Law view as well as on the base plate. Figure 5, right mastoid; Figure 6, left mastoid.

We often find it advisable to add still another view to the conventional angle and the base plates: namely, a posteroanterior projection. The numerous advantages of such an exposure have been expounded by

others. They consist in information about cortical thickness and possibly perforation, about distribution, character, condition of cells, about the petrous portions in a different projection, about defects due to operation and (unfortunately sometimes overlooked) swelling of the overlying soft tissues.

SUMMARY AND CONCLUSIONS

For the purpose of recording the condition of the petrous portions, the submentovertex view (base plate) was added to the standard mastoid examination. Since the base plate also represents a simultaneous symmetrical demonstration of both mastoids on one film, it may conveniently serve for comparing the shadow densities of the two mastoids. Its diagnostic usefulness and reliability in this respect were investigated and found to be of an astonishingly high degree.

The possibility of errors is very small; errors may occur in cases of bilateral affection and can be avoided, as long as the history, the otological findings, and the roentgen findings on the standard films are kept in mind.

An abnormally well visible lateral sinus manifests itself on the base plate as a sharply and regularly outlined round or elliptical area of increased illumination and is of the same pathological significance as on the conventional lateral oblique roentgenograms.

The base plate is a very valuable and reliable supplement to the conventional lateral oblique views, but it can never replace them.

MOTILITY OF THE GASTROINTESTINAL TRACT*

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THE time required for a barium meal to completely traverse the normal gastrointestinal tract, under roentgen observation, has been estimated as twenty-four hours by Groedel,[7] twenty-four to forty-eight hours by Hurst et al.,[8] Walsham and Overend,[9] Carman,[5] thirty-six to forty-eight hours by Brown and Sampson,[3] fifty hours by Case,[6] and seventy-two hours by Bierman.[2] Alvarez and Freedlander[1] recovered and weighed the fractions of a barium meal passed in the stools of normal adults and found that 75 per cent was expelled in seventy-two hours, the residue being passed in the succeeding four or five days. When glass beads, instead of barium, were used the results were approximately the same, as were those of Burnett[4] using millet seeds.

Because of the variation in these and other reports, a study was made to determine a standard transport time for patients admitted to the Third Medical Division of Bellevue Hospital. Subjects included here were free from gastrointestinal pathology, and did not have fever, cachexia or other constitutional ailment which might in any apparent way affect gastrointestinal motility. All were up and about the ward.

METHOD

Twelve hours fasting and twenty-four hours without cathartic, the patient was given a motor meal consisting of 2 ounces of barium sulphate in cooked oatmeal. Six hours after ingestion the position of the head and tail of the column was noted. Two ounces of barium sulphate in fermented milk was then administered to study the esophagus, stomach and duodenum. Thereafter, the patient was on the regular ward diet and no cathartic, enema or other artificial stimulus to defecation was given. An observation was made every twenty-four hours after this until evacuation was complete.

FINDINGS

The head at six hours, in 11.5 per cent, had passed beyond the splenic flexure, in 57.1 per cent it was in the transverse colon, and in 30.8 per cent it was in the cecum and ascending colon. The tail, in 75 per cent, was in the lower ileum, and in 25 per cent in the cecum.

At twenty-four hours, the head, in 27 per cent, had not reached the sigmoid, and in the remaining 73 per cent was in the sigmoid and rectum. The tail, in 89 per cent, had congregated about the cecum, including 6 cases where the terminal ileum was faintly outlined. In the remaining 11 per cent the tail was in the ascending, transverse and descending colons.

The head, at forty-eight hours, in 85.7 per cent, was in the sigmoid and rectum, in the remaining 14.3 per cent it was in the transverse and descending colon. The tail, in 64.3 per cent, was still grouped about the cecum, in 21.3 per cent located in the transverse colon, and the remaining 14.4 per cent were scattered through the descending colon and sigmoid.

At seventy-two hours the head, in 78.7 per cent, was in the rectum, in 21.3 per cent (2 cases) was in the ascending and transverse colon. The tail was, in about equal frequency, found in all parts of the colon.

At ninety-six hours, the head, in 71.4 per cent, was in the sigmoid and rectum, in 28.1 per cent (2 cases) in the transverse and descending colon. The tail was still about equally distributed through the colon.

At 120 hours, the entire series of 52 cases was empty.

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TABLE I

RESULTS OF TWENTY-FOUR HOUR ROENTGENSCOPIC EXAMINATIONS

	6 hr.	24 hr.	48 hr.	72 hr.	96 hr.	120 hr.
HEAD						
Terminal ileum	—	—	—	—	—	
Cecum	8	—	—	—	—	
Ascending colon	8	2	—	—	—	
Transverse colon	30	4	1	1	1	EMPTY
Descending colon	4	7	3	2	1	
Sigmoid	2	8	7	—	3	
Rectum	—	17	17	11	2	
TAIL						
Terminal ileum	39	Tr 6	Tr 2	—	—	
Cecum	13	24	10	1	1	
Ascending colon	—	4	6	3	1	
Transverse colon	—	3	6	4	2	EMPTY
Descending colon	—	1	2	1	1	
Sigmoid	—	—	2	3	2	
Rectum	—	—	—	2	—	
Not examined	—	10	3	4	3	
Empty today	—	4	17	13	8	10
Percentage	—	7.6	32.6	25	15.7	19.1
Empty to date	—	4	21	34	42	52

At ninety-six hours 80 per cent had evacuated, at seventy-two hours 65 per cent, at forty-eight hours 40 per cent, and at twenty-four hours only 7.6 per cent had expelled the meal.

SUMMARY

Fifty-two ambulant ward patients were studied roentgenoscopically to determine the rate of progress, through the gastrointestinal tract, of a barium motor meal. The position was observed six hours following ingestion, and every twenty-four hours thereafter until evacuation was complete.

A few, 7.6 per cent, had evacuated in twenty-four hours, 65.2 per cent had evacuated in seventy-two hours, and the remaining 34.8 per cent was expelled on the fourth and fifth days. The rate of expulsion is prolonged beyond the figures obtained by a similar method of examination in the hands of other observers, but is more nearly in agreement with the experimental results of Alvarez and Freedlander and of Burnett.

The rate of progression and the position of the column were fairly uniform, in all cases, for the first twenty-four hours, but on the later hour examinations were subject to wide variations. At six hours, in the large majority, the column was found between the lower ileum and any portion of the transverse colon. At twenty-four hours, in approximately three-fourths (73 per cent), the entire colon was filled, while in the remaining one-fourth (27 per cent) the sigmoid had not yet been reached.

In only a few cases was the entire meal expelled at one defecation, two, and at times three, acts were necessary for its accomplishment. When the patient defecated, approximately the distal third of the colon was emptied and was not filled again until a mass movement occurred. It is thus seen that after a defecation the position of the remaining column is not a true index of the motility of the column as a whole, and is the explanation for so great a variation in the position of the head recorded in the later hour examinations.

CONCLUSIONS

1. The normal gastrointestinal tract may require 120 hours to completely expel a barium motor meal.

2. This time limit is longer than has

formerly been obtained by a similar method of examination.

3. This time limit is in agreement with experimental results.

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Vol. 39, No. 1

PHYTOBEZOAR

REPORT OF THREE CASES

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MEDICAL writings from almost the beginning of medical literature include reference to concretions found in the alimentary tracts of birds and animals. The ancient materia medica[20] claims "a miraculous property of certain stones to cure disease." The word bezoar signifies counterpoison or antidote and is a term applied to masses found in the stomach of animals and man. The "oriental bezoar stone" of the ancients consisted of a ball of felted hair or vegetable fiber consolidated to a mass, of which the "lapis occidentalis" was obtained from a stag or wild goat of Persia, while the "lapis simiae" came from the Brazilian monkey. The latter, according to the writings of the time, "cost much money as it had great potency." Then, too, the madstone of yesteryear is a memory of not so long ago.

Bezoars are classified according to the material which they contain. The trichobezoar consists entirely of hair; the trichophytobezoar consists of a combination of hair and food remnants; the phytobezoar consists of food remnants entirely; and, finally, there is a more solid type of concretion consisting of shellac, salol, bismuth or similar substance.

It is the purpose of this paper to call attention to the rare occurrence of food concretions in the stomach of man and to report briefly two cases of phytobezoar of the persimmon type and one case of food detritus accumulation erroneously interpreted as a trichophytobezoar or hair ball.

The earliest reported case of a phytobezoar in man is credited to Bucknill by Quain[19] in 1854; the mass was composed of string and cocoanut fibers. A number of other substances composing a phytobezoar are reported: fiber and wood by Hichens and Odgers;[10] wild beets, couch grass and parsley-like plants by Hamdi;[8] salsify by Schreiber;[21] pumpkin, raisins, prunes, celery, tobacco and persimmons by several American authors.

The bezoar consisting entirely of shellac as the result of that solution being used as an intoxicant by painters, furniture factory employees, and others, quoted* as being reported by Friedlander, Vonnegut and Hallas in Germany seems not to have occurred in America. Hamdi's case of a crystallized mass of salol found at necropsy in the stomach of a Turk who had taken large doses of the drug for cystitis, and Hummant's case of a 40-gram mass of bismuth appear to be single instances in the literature.

Persimmons, it appears, are by far the most frequent cause of the phytobezoar—Schulze[22] only dissenting. The rôle of persimmons as the initiating factor in the formation of the phytobezoar seems to be the taking of a liberal quantity of the berry on an empty stomach. Further prerequisites, it appears, are good gastric tone and normal or slightly increased gastric acidity. The persimmon seed may form a part of the mass although its necessity as a nucleus does not appear to be essential. The greater number of cases reported failed to mention the seed as a constituent. No seed was present in the mass of either case reported here. The gum and jelly forming constituents, together with the small cellulose content are sufficient, it appears, for the molding of an insoluble mass in the stomach, and it is generally agreed that it is formed soon after ingestion. While other food elements may be added during its stay in the stomach, the persimmon bezoar presents no lamination to suggest such additions. As pointed out by a number of authors, the comparatively frequent occur-

* Mentioned in articles by Hart[9], Balfour and Good,[1] Smith,[23] and others.

rence of the concretion following the rapid eating of the berry without other food, particularly by hunters or trampers is no doubt significant.

Balfour and Good[1] point out that the most favored geographic distribution of the persimmon tree covers a band extending eastward to the Atlantic coast from Oklahoma, Kansas and southern Nebraska. The cases on record are chiefly from this area.

Regarding the frequency of the persimmon bezoar, Hart,[9] in 1923, reported 8 cases Balfour and Good,[1] in 1929, reported a case and reviewed 14 to bring the total to 15. Smith,[23] in 1932, reported 2 cases and estimated a total of 50 in the literature. Murdock,[14] in 1934, added one case of his own and reported 12 others in the region of Tulsa, Oklahoma. Murdock's report brought the total to 63 cases, to which we wish to add 3 cases, 2 of which were true persimmon bezoars and the third consisted of vegetable skins and food detritus. The latter case is similar to the cases reported by Bryan[2] and Upson[24]—the only other cases a fairly complete review of the literature has revealed.

Of the 39 cases in the British and American literature reviewed, 33 cases occurred in men and 6 in women. The age of the patient at the time of discovery of the bezoar, as given in 35 cases, ranged from four to seventy-five years, the average being 42.7 years. In 23 cases the shortest time from ingestion of persimmons to operation was two days and the longest 395 days, the average being 120 days. Droegemueller[6] reports a case who gave a history of gastric symptoms covering a six-year period and Smith's[23] case gave a history of eating the berry "some years" previously. The onset of symptoms following ingestion of persimmons is usually given as varying from immediate to a few hours. Ulcer is mentioned in 9 of 39 cases reviewed.

The 2 cases of persimmon bezoar reported herewith were males, seventy-one and seventy-five years of age respectively. The phytobezoar was accompanied by gastric ulcer and hematemesis in each instance. In one of our cases the ulcer undoubtedly antedated the eating of persimmons, while the concretion may have produced the ulcer in the second case. In the latter case, the ulcer had been surgically repaired without discovery of the foreign body. An ulcer of the duodenum with perforation existed in our third case and no doubt contributed mechanically to the formation of the foreign body.

DIAGNOSIS

The usual complaints of the patient are a vague fullness, gas, nausea and vomiting, paroxysms of upper abdominal pain, and the sensation of a lump in the upper abdomen. Frequently the patient feels a movable lump which alternately appears and disappears. Purging is occasionally a complaint and in those cases complicated by ulcer, severe hematemesis may be a feature. The vomiting of a watery brown fluid is occasionally reported. Intestinal obstruction has occurred when a large fragment has passed from the stomach; and the appearance of small fragments of disintegrating bezoar in the stool has been reported. Pain occasioned by the spastic seizure of the mass in the empty stomach may be relieved by the taking of fluids.

The actual diagnosis of persimmon bezoar depends on the roentgenographic finding of an intragastric translucency, usually quite free to the palpating fingers and over which the opaque medium may be roentgenoscopically manipulated. Occasionally gastrospasm may hold the bezoar firmly or displace it into the cardiac segment. The review of the cases reported indicates that the relative infrequency of the lesion, and the failure to obtain a history of persimmon eating, accounts for a fairly high percentage of incorrect interpretations of the findings. As reported by Droegemueller,[6] and Hart,[9] and as illustrated in Case 1 below, palpation at laparotomy may fail to disclose evidence of the mass in the stomach. Therefore in those cases diagnosed as tumor of the stomach, wherein the clinical

features are not entirely in harmony, the possible existence of a bezoar should be considered.

REPORT OF CASES

Case 1. C. K., an unemployed white man, aged seventy-one, a patient of Dr. Joseph Welker, entered the hospital on January 30, 1935, complaining of gas and belching, the feeling of a lump in the stomach and epigastric pain.

In June, 1934, the patient had had severe pain in the epigastrium and was taken to a hospital where he was operated on for a perforated gastric ulcer. He recovered slowly and vomited a great deal. His discomfort bore no relation to meals, although soda gave relief at times. Four months before this admission, and occasionally since, he has felt a lump in his stomach. His previous general health had always been good.

Physical examination revealed a well-developed, poorly nourished, somewhat emaciated white man. The abdominal wall was relaxed. A palpable, slightly movable mass existed in the epigastrium which was best felt with the patient standing and which was not tender.

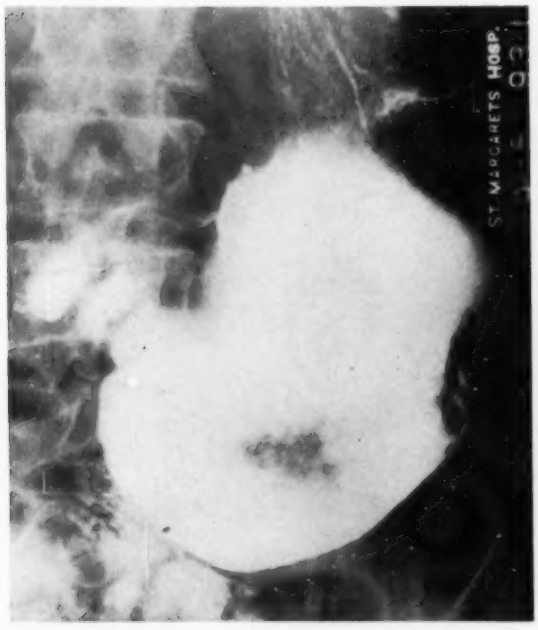

Fig. 1. Case 1. Patient standing. Phytobezoar produces area of translucency in dependent portion of the stomach. Surgical repair of a perforated ulcer on anterior prepyloric wall six months previously.

Fig. 2. Case 1. Photograph of phytobezoar; weight 110 grams.

The blood pressure was 130/70; the peripheral vessels were sclerotic. There was a marked arcus senilis; the pupils were irregular, the left larger than the right and each reacted sluggishly to light. The remaining teeth were carious. There were no pathological reflexes. The Wassermann reaction was negative. Hemoglobin, 48 per cent; red blood cells, 3,980,000; white blood cells, 12,500; polymorphonuclears, 83 per cent. Stool positive for blood. Gastric analysis: average total acidity 40, free HCl 27, benzidine test for blood positive.

Roentgenographic study of the stomach showed a 25 per cent residue at six hours. The stomach was medium in size, oblique in position, presented a rounded negative shadow, somewhat smaller than a fist, in the dependent portion which could be displaced into the cardiac portion without discomfort. The immediate prepyloric area showed an intermittent, irregular, tubular appearance over which peristalsis was interrupted. The pyloric segment was fixed in position. The deformity of the prepyloric area was interpreted as gastrospasm superimposed on the deformity produced by the surgical repair of the old ulcer; and the negative shadow, as a phytobezoar.

When specifically questioned, the patient stated he was very fond of persimmons and had eaten liberally thereof, in the fall of 1933, but none since. This date was therefore seven or eight months before his operation for ulcer and fourteen months prior to this admission.

On February 12, 1935, a gastrotomy was performed by Dr. C. C. Nesselrode. The pyloric antrum presented the scar of previous closure. On opening the stomach, a dark brown mass 10 cm. in length by 5 cm. in diameter was found and removed. The mass weighed 110

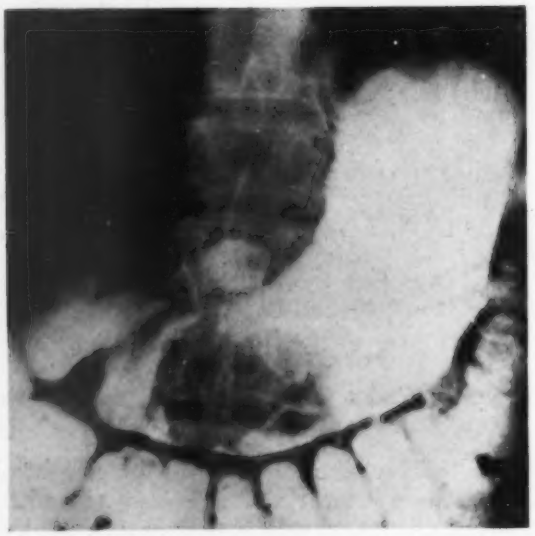

Fig. 3. Case II. Patient semi-prone. Phytobezoar produces area of translucency in dependent portion of the stomach. Accessory pocket of gastric ulcer seen at the lesser curvature.

grams and possessed a sour odor. Its surface was rough, pitted and resembled an Irish potato. When the black outer layer was chipped off, the inner surface presented a lighter brown gummy appearance without definite architecture. Inspection of the stomach revealed no ulcer. The pathologist's conclusion was phytobezoar.

was present in the stomach fourteen months and may have produced the ulcer which had been repaired.

Case II. H. C. G., a white farmer, aged seventy-five, a patient of Dr. Jess Young, was admitted to the hospital on December 25, 1934. He complained of severe pain in the upper abdomen, vomiting of blood and tarry stools. He gave a history of occasional trouble with his stomach for thirty years, during which he vomited, had a large amount of gas, and obtained some relief from soda. He had felt very well for about a year until one night about three weeks before admission when he suffered severe pain in his upper abdomen. This pain was not relieved by food or soda. He became progressively weaker. Finally, three days before admission, on arising from bed, he vomited, without nausea, a large amount of bright red blood and some dark blood. He fainted and later passed numerous tarry stools. On the following day he again fainted and later passed other tarry stools.

Examination revealed a well-developed, poorly nourished, very anemic white man. Moderate tenderness and tenseness of the entire upper abdomen was present. A palpable movable mass about the size of a large lemon was felt in the epigastrium. Hemoglobin 33 per cent; red blood cells 1,560,000; urine showed a trace of albumin.

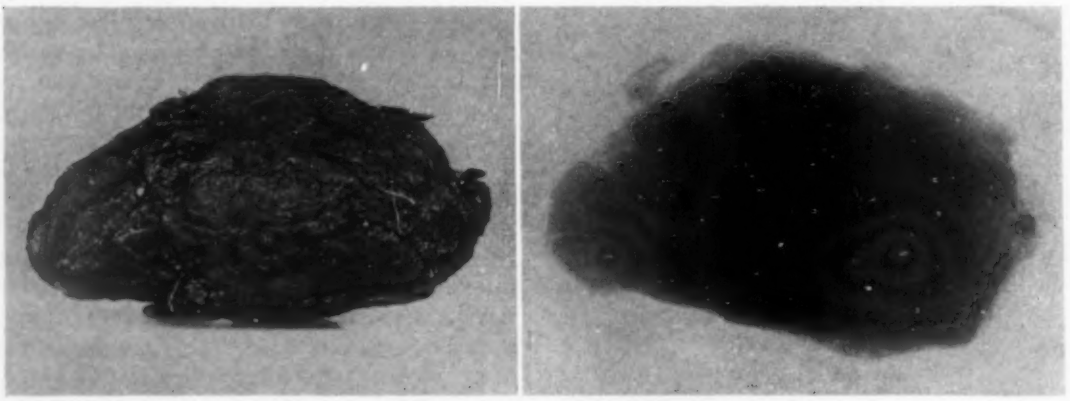

Fig. 4. Case II. Photograph and roentgenogram of phytobezoar; weight 89 grams.

Recovery was delayed, nausea and abdominal distress continued. The patient gradually improved, however, and left the hospital on March 27, 1935. Complete recovery and good health is reported in December, 1935.

It appears rational to believe that the bezoar

The roentgen examination of the stomach on December 26, 1934, six hours after the motor meal, showed the stomach empty, the head of the column at the splenic flexure. The stomach was medium in size, oblique in position. The pyloric antrum presented an intermittent,

tubular appearance and a deep accessory pocket on the posterior gastric wall. A palpable mass did not correspond to the antral constriction. The patient was very weak, could not stand manipulation and the barium-filled splenic flexure confused the roentgenoscopic picture.

Two days later the examination was repeated after a series of cleansing enemas. The mass was again palpated and seen as a negative shadow against the opaque meal and was obviously free in the stomach. The deep accessory pocket on the posterior gastric wall was again observed.

On specific questioning, the patient stated that a few days before the onset of his present illness, he had procured a large quantity of persimmons and in the course of two or three days had eaten several dozen.

A conclusion of persimmon bezoar and penetrating gastric ulcer was made.

The patient was given three blood transfusions in the interval and on January 7, 1935, a gastrotomy was performed by Dr. Young and Dr. Denman. An oval, somewhat irregular phytobezoar was removed, measuring 8.5 cm. by 4.5 cm., and weighing 89 grams. The patient stood the operation poorly, so that a careful survey of the stomach was not attempted. At the end of a week he appeared improved; hemoglobin 57 per cent; red blood cells 3,530,000. On January 18 he was able to be up in a chair and was dismissed by ambulance.

The patient was reported as having died a cardiac death in July, 1935, six months after leaving the hospital. An autopsy was not obtained.

Case III. M. A., housewife, aged sixty-five, a patient of Dr. E. L. Asbell, was admitted to the hospital on October 2, 1934. Her complaints consisted of nausea, vomiting, diarrhea, a lump in her stomach, discomfort after meals and the loss of 30 pounds in weight during a six-week period.

Her illness began eleven months ago, on November 25, 1933. Following a heavy meal on that date, she vomited several times, and complained of discomfort in the epigastrium for two or three days. A similar, though milder attack followed one month later.

On September 1, 1934, one month before admission, while riding across state in an automobile, she experienced a sudden sharp pain in the upper abdomen. She felt faint, perspired freely and vomited. She was taken to the nearest town where a physician told her she had a perforated ulcer and advised that she return to the city for operation. The physician's advice was not followed and the patient returned home. Her condition did not improve and she was brought to the hospital.

Fig. 5. Case III. Patient prone. Rounded opaque mass in the stomach at twenty-four hour interval. Note also pressure deformity at hepatic flexure by inflammatory mass in the right upper abdomen. Compare with Figure 6.

Examination revealed an obese white female, teeth out, pharynx injected; pupils equal, reacted to light sluggishly. The cervical nodes were palpable on each side. The upper abdomen was tense and tender and the right upper abdomen rigid. An irregular, somewhat indefinite mass was palpable at the right costal margin and inferiorly for about four fingers. The mass moved with respiration.

On the day following admission the stomach was examined roentgenographically six hours after a motor meal at which time the stomach contained a small residue and the head of the column was at the mid-ascending colon. The cecum was normally free. The stomach filled readily, was long, moderately increased in size, displaced to the left and the pyloric end ro-

Fig. 6. Case III. Patient semi-inverted. The opaque mass falls into the cardiac portion of the stomach.

tated posteriorly, compressed and firmly fixed to an obviously inflammatory mass in the right upper abdomen. A trickle of the medium through the flattened duodenum could be seen, but an ulcer crater was not identified.

On the following day at the twenty-four hour interval, the colon was incompletely filled, the hepatic flexure displaced inferiorly by the mass in the right upper abdomen. In the left upper

Fig. 7. Case III. The mass is included when a few swallows of opaque medium are taken, a halo separating the opacities. Patient prone.

Fig. 8. Case III. When the patient is placed in a semi-standing position, the mass falls, again outlined by a halo due to a nonopaque periphery.

Fig. 9. Case III. Four days after taking barium, the mass, indicated by arrows, retains a fraction of the opaque medium.

abdomen there was a rounded barium-contained shadow about 5 cm. in diameter. Manipulation of this mass proved that it was free in the stomach and unrelated to the mass in the right upper abdomen. The mass was surrounded by a narrow halo of nonopaque material, as shown by the administration of additional opaque medium (see Figs. 7 and 8).

At this point in discussing the problem with the grown daughters, we were told that one of the family's concerns was the patient's habit of holding her hair in her mouth.

Observation of the barium-contained shadow was repeated, through the fifth day, at which time a small amount of barium could still be seen in the ill-defined mass in the stomach (see Fig. 9). During this period the patient suffered chiefly from nausea, vomiting and restlessness. Her appetite was poor, she vomited a large amount of fluid and practically all food from one to three hours after eating.

A diagnosis of a small hair ball in the stomach and extensive inflammatory mass in the upper right abdomen seemed rational.

On October 9, 1934, a laparotomy was performed by Dr. C. C. Nesselrode. On opening the abdomen "an inflammatory mass was found involving the greater curvature of the stomach, the gastrocolic omentum, the entire gallbladder and was adherent to the anterior parietal peritoneum at the right of the midline. No effort was made to interfere with this inflamed mass. The stomach was opened and a large amount of green colored flakes, apparently food residue, was sponged out."

The pathological report described "a number of pieces 1.5 by 1.5 by 0.1 cm., grayish in color, soft, cellular and friable, presenting no definite architecture and somewhat gelatinous in appearance." Microscopic sections showed "a gummy, granular, bluish staining mass, with irregular, large cell masses, apparently composed of plant cells." The pathologist's conclusion: "amorphous cellular mass, probably food material."

The patient was in shock following the operation. She improved somewhat, but continued to be cyanotic at times. There was little vomiting, but the pulse became irregular and on the sixth postoperative day, she developed some air hunger and edema of her feet and legs. The temperature remained high; drainage which had at first been bloody and serous, became purulent, then foul. She died on the twelfth postoperative day.

Post-mortem examination revealed a perforated duodenal ulcer with extensive localized abscesses extending to the right around the gallbladder, then inferiorly behind the ascending colon, also to the left posterior to the stomach and inferiorly behind the descending colon. Death was due to a generalized peritonitis and myocardial decompensation associated with both an acute and chronic nephritis.

SUMMARY

1. The literature on phytobezoar is briefly reviewed.

2. Two cases of phytobezoar of the persimmon type are reported.

3. One case of food detritus accumulation erroneously interpreted as a tricophytobezoar is reported.

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THE USE OF RADIUM AND ROENTGEN IRRADIATION IN BENIGN HYPERTROPHY AND CANCER OF THE PROSTATE*

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SINCE there is a dearth of material concerning the radiation treatment of benign hypertrophy and cancer of the prostate, I consented to write a paper on this subject at the insistence of the Chairman of the Program Committee.

My material is taken from the records of the Howard A. Kelly Hospital and represents the work of Drs. Howard A. Kelly, William Neill, Jr., and myself.

BENIGN HYPERTROPHY OF THE PROSTATE

Attempts at reducing the size of prostatic adenomas by radium or roentgen therapy, and thereby relieving urinary obstruction, have been made since the beginning of the century. These endeavors have met with no marked welcome from urologists. This is readily understandable when one considers the immense obstacles that have been surmounted in developing the present surgical methods, and the generally satisfactory results obtained by them. In no field of medicine has there been greater activity and more substantial accomplishment than in urology during this century. That there are cases in which safer and simpler methods, if available, would be used is evidenced by the prostatic massage, enemas and irrigations used in some early cases, and then there are those patients seriously impaired by age, general disease and other complications. Irradiation by roentgen rays and radium has been tried and reported on by comparatively few observers in recent years, but the results are good enough to merit studying the methods employed.

Experimental work on a number of animals—rats, dogs, monkeys, etc.—has shown that conditions closely resembling spontaneous hypertrophy, and leading to urinary obstruction, can be produced by hypodermic injections of the female and male sex hormones, and that by the addition of other antagonistic hormones the effects can be reversed. The testicles and the pituitary gland, so far as is known, are the principal internal secretory glands involved.

Actual clinical employment of endocrine substances, with favorable results in a considerable percentage of the cases treated, have been reported by Lower and McCullagh,[15] Van Cappellen,[25] and Laqueur.[14] This has lent new impetus to the controversy as to whether prostatic hypertrophy is a hypertrophy or a true adenoma, it being frequently assumed that true adenoma cannot be influenced or caused by endocrine substances. There are, of course, several examples to show that they can be so affected.

Prostatic hypertrophy does not predispose to cancer, as will be referred to in a later paragraph. It is dangerous solely because it leads to obstruction to urinary flow and the consequent effects on the urinary bladder and kidneys. Randall[19] has written a monograph on the pathological anatomy, which should be read by everyone who wishes to clearly visualize the disease. To differentiate prostatic hypertrophy clinically from cancer and other obstructions demands thorough urological training in the proper assessment of the facts of the history, the use of the cystoscope and the ability to use the modern refined methods of estimating vesical and renal functions and impairments. In other words, the radiologist should have, if he treats these cases, the full cooperation of a competent urologist. Hemorrhage and local

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pain are almost as frequent with simple hypertrophy as with cancer of the prostate. The age incidence is similar to that of cancer. The studies of Randall[19] and Moore[16] indicate that the percentage frequency increases almost exponentially from the fourth decade until extreme old age, when it is nearly 100 per cent.

Of course, not all hypertrophies cause obstruction; many cease growing, some actually recede. It is certainly not true, as is sometimes stated, that all progress continuously.

Among reports in the literature are those of Burnam and Neill[6] and Barringer, Dean, Herendeen and Duffy,[3] Schiller and Altschul,[22] Henningsen,[13] and Abel.[1]

Burnam and Neill report 29 cases treated by teleradium therapy, with favorable results in 17. The technique will be described in a later paragraph.

Barringer et al. noted marked relief in more than 30 per cent of their cases. There were reductions in size of gland, relief of dysuria, and reduction of residual urine. The agent used was roentgen rays and the dosage was mild, through three portals. These authors attribute the relief to an effect which caused the edema of the gland to disappear.

Schiller and Altschul report on 9 advanced cases with retention, and use slightly greater roentgen-ray dosage than Barringer. Their results are favorable.

Henningsen's contribution is an interesting one. He contends that roentgen irradiation is of little value, but that very advanced and operatively unfavorable cases, of which he reports on 11, were improved by intravesical radium. In 4 acute retentions, 2 were relieved. He puts 2 mg. of radium in a special retention catheter, which is left in for ten days. The total dose is about 500 mg-hr.

Abel reports on 56 cases, of which 35 have been adequately treated and followed. He uses seven portals and in his first series gives each field, taking about one week, two-thirds of an erythema dose. Of the 35 cases, 26 were subjectively relieved, and in most cases there was relief complete from the retention and enlargement. Prostatectomy is reserved for cases which do not respond to this roentgen treatment.

Our own material covers a period from April, 1913, to January, 1932, and consists of 68 patients. The ages varied between forty and eighty-six years. Very little conclusive evidence can be added to the report of Burnam and Neill made thirteen years ago. Marked relief was obtained in 30 cases, freedom from dysuria, retention, hemorrhage, and reduction in size of the prostate were observed. Many of these cases were in advanced stages, with retention. Twenty-two cases were not materially benefited. Six, all early cases, were improved, but disappeared from observation within a few months of treatment. Among some of the failures, there was marked reduction in the size of the prostate, but no relief of the retention. Three cases, completely relieved, had return of symptoms after five years, and then prostatectomy. One case, with complete retention, was relieved for sixteen years.

It has been difficult to obtain accurate data. Most of the patients were old, and deaths from other than prostatic causes have occurred in a number. The treatments have varied from 10 gram-hours perineal to 60 gram-hours through three portals. Practically all of this group have been treated by teleradium therapy alone. Improvement of dysuria has been slower than in the cancerous group, varying from one week to one month after conpletion of series of treatments.

Summary and Conclusions. By means of radiation given in a series of treatments, more than 50 per cent of the patients received relief symptomatically, as well as from the standpoint of objective findings (reduction in size of the tumor, relief of residual urine, improvement in functional renal tests). This improvement, from a single series of treatments, may be for only a few years. Some patients respond satisfactorily to very little treatment; others require more. It is well to begin with mild

exposures and to avoid temporary swelling. Ill patients, with complete retentions, high blood nitrogen and infections, must be hospitalized and treated as if prostatectomy were being prepared for.

Very intensive treatment, such as is used in cancer cases, has not been reported in the literature. Possibly much better results could be obtained by it than by the mild procedures employed.

CANCER OF THE PROSTATE

With the limited time at my disposal, it is impossible even to skim through the pathology, symptomatology and differential diagnosis.

The majority of prostatic cancers are adenocarcinomas. Metastases to the seminal vessels and regional lymph glands are common. The disease is often associated with hypertrophy, but is not derived from it. The recent anatomical investigations of Moore[16] confirm this view, as well as demonstrate that 75 per cent of the cancers develop in the posterior lobes. These are important data in their bearing on both diagnosis and treatment.

Von Recklinghausen[20] (1891) was the first to note the frequency of metastases to the pelvis and lumbar vertebrae. This localization, as demonstrated by Warren, Harris and Graves,[26] is due to extensions along the perineural lymphatics, in addition to blood transportation. This work explains also the marked pain present in cases without bone involvement. Metastases to these bones is very common, and, in most cases, can be demonstrated by roentgenograms. The osteoplastic type of metastasis predominates. Gutman, Sproul and Gutman[11] showed that this is probably due to the formation of phosphatase by the tumor cells. The earliest discomfort may be from metastasis. Obstructive and other symptoms are the same as those in prostatic hypertrophy and other urological conditions.

Diagnostically, induration and nodulation by rectal examination are the chief differential features as compared with simple hypertrophy. Cystoscopic examination is not a very helpful differential method, but narrowing and rigidity of the prostatic urethra is. Barringer attaches great importance to diagnostic aspiration biopsy.

Duration of Life in Cancer of the Prostate. There is a complete absence of authentic data as to the minimum, maximum and average times that elapse between the onset of the disease and the appearance of the first symptoms. Some authors hold that this is a period of months, or even years; other take exactly the opposite view. These opinions seem to be largely personal, unsupported by proof. The large percentages of microscopical prostatic cancer, demonstrated in the autopsy materials of Moore[16] and Rich,[21] are suggestive that the growths may be slower than adenocarcinomas in other organs. The small number of cases that survive five years from the onset of symptoms is evidence to the contrary.

After the onset of symptoms, Bumpus[5] finds, in 71 cases without demonstrable metastases, that the average length of life is 3.4 years. Hager and Hoffmann,[12] in 396 cases, find that 47 per cent died within one year.

It should be remembered that long duration of symptoms may be due to pre-existent hypertrophy, or other urological conditions which have preceded the cancer.

Under these conditions, it is not possible to determine the average effect on prolongation of life from irradiation. This applies to comparisons with non-treated cases, or those treated by conservative surgery.

It is frequently stated that the cancers of the prostate are rapidly growing in the young—that is, in those under fifty years of age—and that the converse is true for very old men. Probably, by percentage, this is true, but it should be borne in mind that there are many exceptions in each instance. Barringer believes that approximately 10 per cent of these cancers are anaplastic and rapidly growing.

Incidence of Cancer of the Prostate. The

commonest age for cancer of the prostate is between sixty and seventy years. It is frequent between fifty and sixty years. Apparently decreasing after seventy, it actually steadily increases in proportion to the population of men in any decade. This is best demonstrated by Moore's studies. Under fifty it is rare, about 3 per cent; in our own series of 158 cases, 2 were between forty and fifty, and 2 under forty (thirty-seven and thirty-eight years old). Spath[24] reports a case in a boy of 6¾ years, and reviews the literature of cases under forty years of age.

Results of Treatment of Cancer of the Prostate. The modern treatment of prostatic cancer is of comparatively recent date. Only two decades ago, there was little to do for the prostatic cancer sufferer, other than to resort to catheter, or to suprapubic drainage for obstruction, and to use opium to alleviate the pain. Even today, some of the leading urologists feel that this is the most merciful and effectual procedure.

Most special workers, however, have not been content with this "laissez faire" policy, and, like workers in cancer in other fields, are insisting on early diagnosis and radical treatment, aiming at permanent cure. How far this can be carried is a question for the future. Our means of investigation, even if experts were periodically examining the entire male population, would permit of only a moderate gain in number of early symptomless cases discovered. By far the best results obtained have been with these early cases, with cures obtained either by radical surgical removal, or by the surgical application of radium interstitially to the growth, with or without the addition of roentgen irradiation.

Obviously, surgery of a possibly curative nature is limited to cancer still within the prostatic capsule. Young,[28] a pioneer in this field, devised a perineal operation in 1907. In 1936, he reported a 53 per cent five-year cure rate, and 4 per cent primary mortality. His cured cases number 17. Belt[4] has done the same operation in 25 cases. Eighteen proved to be microscopically confined to the tissues removed, and 10 are living and apparently free of disease. In 7 of his cases, the disease went microscopically beyond the tissues removed. These were given high voltage roentgen treatment, 600 to 900 kv. by Mudd; all are living and apparently free of disease for from one to three years.

The first reported use of radium was by Pasteau and de Grais[18] (1913). They record improvement in 2 cases from intravesical radium therapy. Young, by 1926, had used this method in 82 cases, often combining it with intrarectal and external roentgen treatments. He noted improvement, both symptomatic and objective, but records no complete reliefs which might be termed cures.

Chauvin[7] reports 39 cases. He exposes the prostate by the perineal route, introduces a series of needles containing in all from 24 to 36 mg. radium, and leaves them from eight to twelve days. He has observed local cure in 94 per cent of his cases, but does not give longer durations than two years and, further, makes supplemental report in 1935 as to late results.

Fruchaud[9,10] uses a similar method, with smaller dosage—eight days, with from 20 to 30 mg. Both of these authors note that only 50 per cent relief of obstruction is obtained. During the treatment, urinary flow is maintained either by a retention catheter or by a suprapubic opening. Fruchaud does not give a statistical study of results, but has had one cure of more than five years.

A series of most interesting contributions has been made to this subject over a period of years by Barringer. In 1936,[2] he reports 20 cases well from every clinical standpoint; one, more than five years. This represents 5.7 per cent of his large treated material. Four of these cases have been well for ten years or more. Out of the entire group, Barringer feels that only 16 cases were in the early operable class where surgery might have been employed. It is obvious, therefore, that some of his cured

cases must have been in patients with advanced cancer. Dr. Barringer's technique is well known and consists of implantation of needles through the perineum, through the posterior lobes, and into lateral and median lobes, through a suprapubic opening. His dosage to the posterior lobes is from 1,500 to 1,800 mg-hr., and the needle implants are on the basis of 1 mc. to each cubic centimeter. In his recent 1935 and 1936 publications, he advocates the additional employment of teleradium therapy.

Most cancers of the prostate are far advanced when the patients first seek medical aid. To this day, some urologists do nothing but treat symptoms as they arise. Most special workers in this branch of medicine are not and have not been content with analgesics for pain, the use of catheter for obstruction, and the final suprapubic drainage. The advent of the cystoscopically controlled methods of electrical resection has been a marvelous boon in relieving obstruction, making life comfortable and certainly prolonging life by removing some of the secondary causes of death.

Partial or euphemistically conservative prostatectomy, whether suprapubic or perineal, has the same effect, but is more dangerous and more likely to speed the rate of growth.

Surgery is out of the question in huge, advanced growths and at the moment, the only recourse is irradiation. Reliance on radium implantation of such a growth brings up the questions of what the effects will be as to cure, as to palliation of the symptoms, as to injuries, as to prolongation of useful life. Obviously, it is not applicable to cases showing determinable bone or visceral metastases. Can anything be done for these cases? What can be done by cross-firing with roentgen rays or teleradium?

Dossot,[29] reviewing the vast material of the Neckar Clinic, says that radium and roentgen irradiation are of little value.

Smith and Peirson,[23] reporting on 25 cases from the Massachusetts General Hospital, noted decrease in pain from metastases, but not much improvement in vesical discomfort.

Widmann[27] comprehensively reviews the literature and reports on 152 cases treated by roentgen irradiation. He notes marked relief of pain, hemorrhage and dysuria for varying periods, from a month to many months. In many cases, there were observed marked recessive changes in the tumors, but no complete disappearances. Ferguson[9] has had similar experiences and has given, very carefully, details as to the character of treatment and results.

Mudd and Emery[17] report three and a half years' experience, using nine portals of entry with the 600 to 900 kv. machine of the California Institute of Technology. Of these, 33 per cent had bone metastases and did not stand full treatment. In the remaining 22 cases, there was tremendous shrinkage of the mass, and in a number complete disappearance. Cystitis and proctitis were common, and some skin injuries. I examined some of these cases in the fall of 1934, and was impressed by the effect on the tumors. The patients were all ambulatory and obstruction, where present, had been relieved by resection.

Belt[4] states that the California Institute of Technology has treated 36 of his private cases, of which 7 have already been referred to under earlier cases. A second group of 14 cases had had preliminary conservative prostatectomy for obstruction. Only 2 are living, one of whom is dying with cancer and the other was treated only eight months ago. Belt's most interesting cases are in a third group, 18 in all, where preliminary resection was done to relieve the obstruction. Some of these are quite recent (9 cases) treated for more than two and a half years, and 4 of these are in very good condition.

No cases are reported in the literature giving the combined effects of radium implantation and roentgen treatment.

Summarizing, it is evident that a number of cases treated by roentgen irradiation have had marked relief of symptoms and, in many cases, marked reduction in

the size of the cancerous mass, but that no cures have been reported, except by Barringer and possibly by Mudd and Emery.

As to our personal material, it comprises 158 cases, investigated and treated between April, 1912, and January, 1932. One hundred and twenty-five were treated by teleradium therapy alone, and the remaining 33 by methods to be described briefly. With a single exception, all were very advanced. The early case had a total removal of the prostate and seminal vesicals by Marion's method. This patient survived and was clinically well for four years and then died at the end of five years from metastases. Fifty-nine cases, or 38.6 per cent, had demonstrable metastases on the first visit. Of the remaining 98 cases, many had complete obstruction; others, severe dysuria, pain, hematuria, etc. Only 10 had tumor alone as a symptom. Nine cases were observed who had had prostatectomy from one to sixteen years previously for benign hypertrophy, and with microscopical diagnosis of prostatic hypertrophy, which means that an intracapsular prostatectomy does not remove the possibility of prostatic cancer developing later.

To afford some basis for determining the amount of palliation secured, I have arbitrarily divided my cases into three groups:

First, those questionably improved, and with these, I have placed those improved, perhaps entirely clinically relieved, but only for a few months.

Second, those completely relieved symptomatically and with objective findings, such as reduction in the size of the tumor, and improvements in renal function for more than one year. Sixty-five cases fall in this group, some of which are among the metastatic cases.

Third, those completely relieved for longer than three years. There are 17 cases in this group, in addition to the early case already described. None of these cases was in the metastatic group. All showed not only clinical relief of discomfort, but great shrinkage in the size of the tumors. Nine had recurrences after the third year and all were dead before the fifth year. Four seemed perfectly well for four years and died of metastasis or recurrence before the sixth year. One was clinically free of symptoms and by palpation the prostate was almost normal five years after treatment. The patient was then lost sight of.

One patient lived nine years, but had recurrence locally and by metastases at the end of seven years.

The 2 remaining cases appear to be permanent cures. The first, a man aged sixty, had been treated six months before by an intracapsular prostatectomy for what proved to be a carcinoma. At the time of his first visit, January 5, 1925, he appeared very ill, had lost a great deal of weight, had dysuria and hematuria, and a huge infiltrating mass. His blood chemistry was normal and the roentgen findings were negative. Between January 8 and March 30, 1924, he received, through multiple portals, a total of 120 gram-hours of radium at a distance. In about four months, all discomfort, as well as the mass, had disappeared. He remains apparently quite well up to the present time.

In a second case, a man aged fifty-two, the vesical symptoms had been present for a year. Eight months previously, partial suprapubic prostatectomy for an obstruction had been carried out. Only partial relief followed this procedure and when first seen, October 23, 1930, this patient had marked dysuria, pain and infection in the bladder. Examination disclosed a large, hard mass. Within two weeks, the treatment, consisting of 80 gram-hours irradiation at a distance and 1 gram-hour interstitial exposure by means of needles introduced through the perineum, was given. Within eight weeks the patient was well, both clinically and subjectively. A recent (1937) communication from this patient indicates perfect health, but no examination has been made in five years. He is living abroad.

Out of the entire 158 cases, we have either lost sight of, or have given only one treatment to a total of 49 patients. These

are all classified "dead from the disease," although some of them were in good condition when last seen.

Teleradium Technique. Up to 1921, about ten years, we employed the open pack method of teleradium therapy, using skin distances of from 7.5 to 10 cm., giving, through multiple portals and within two weeks to three months, a total of from 100 to 300 gm-hr. The variations depended largely on the condition of the patient. For the last ten years of the period under consideration, we used a teleradium apparatus with similar conditions as to distance and dosage.

In 33 cases, other methods than teleradium were employed, either as additional procedures, or alone.

Our first case (1912) was treated by intrarectal and intravesical radium therapy.

Our second case (1913) was treated by opening into the growth through the perineum and giving 6 gm-hr. in a single exposure. This is the only case where death seems definitely due to the treatment.

In 13 cases, teleradium was combined with intravesical and intrarectal applications of radium.

In 4 cases, the first in 1915, radium therapy alone by operative implantation was carried out.

In 4 of the later cases, teleradium and roentgen therapy were combined.

In 9 cases, implantations of radium were combined with teleradium therapy.

In 1 case (1914) intravesical radium therapy was given through a suprapubic opening.

General Impression and Conclusions on the Treatment of Cancer of the Prostate.

(1) Improvement in absolute cure percentages in the future will depend on discovering and treating the disease in its incipiency and early stages.

(2) Prostatic cancers vary greatly in their sensitivity to radiation and in their malignancy.

(3) Intravesical and intrarectal treatments are, from the physical standpoints of dosage, inadequate when employed alone, and limit the use of better methods when combined with them. This is particularly true from the viewpoint of palliation. Even with objective improvements symptomatically, the patients are often made more uncomfortable.

(4) Cross-firing with radium at a distance, or, as we now feel is equally as good, with roentgen rays, is the most valuable palliative method at our disposal and may actually bring about cure in a few of the cases beyond any possibility of operative treatment.

(5) Radium implantations should be reserved for use in cases presenting a possibility of cure. This excludes the metastatic cases and the huge growths.

(6) In all cases where either operation or implantation is considered such procedure should be preceded by an adequate irradiation such as is now used in mammary cancer, and it should be considered as a postoperative and postimplantation procedure in some cases.

(7) Obstruction, necessitating catheterization, and not promptly relieved by irradiation, should be treated by electrosurgical resection as a preliminary to further irradiation.

(8) Metastatic cases should be treated, as marked palliation can often be secured, relief of pain being the outstanding feature.

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DISCUSSION

DR. BENJAMIN S. BARRINGER, New York City. I have some lantern slides which I think will make my discussion of Dr. Burnam's paper clearer. Before we can intelligently irradiate a prostate we must understand its anatomy. (Slide) You see here a cross-section of a normal prostate showing the bladder end, the urethra, the ejaculatory duct and the various lobes. I wish to draw particular attention to the posterior lobe which is away beneath the bladder neck. If you seek to determine the origin of prostatic carcinoma I think you will find that in the large majority of cases it starts in this posterior lobe beneath the bladder neck. When the patients come to us the carcinoma has spread, in the majority of cases, to the lateral and possibly the median lobes. In certain cases the carcinoma arises simultaneously in the posterior, lateral and subcervical group.

A word about aspiration biopsy. I have long felt that if you report a series of cases of cancer without pathologic examination it will be said that you are wrong in your diagnosis. For a long time we struggled with aspiration biopsy, until Dr. Martin of Memorial Hospital successfully aspirated carcinomatous glands of the neck. His method we employ in cancer of the prostate. The patient is placed in the lithotomy position, the finger in the rectum, and with an aspirating needle material from the suspected lobe is obtained. The needle is placed in the prostate, withdrawn, and pushed through in another direction with an attempt to cut off the section (indicating). The material

is put on a glass slide and the diagnosis is made rapidly if there is sufficient tissue and if the pathologist is trained in the method. You do not get two or three or half a dozen cells as so many think but a good piece of tissue. This lantern slide shows carcinoma of the prostate. I show this simply to emphasize the point that sufficient material is obtained in this manner for a definite diagnosis.

The radical resection by Young for carcinoma of the prostate is a beautiful operation and, as Dr. Burnam said, Young is a pioneer in this field. I think he has operated on about 30 cases in that many years. When we consider that only about one case is operated upon in this way a year I do not believe that the problem of prostatic cancer is solved. What happens to the large amount of other material that passes through his hands?

As to deep roentgen therapy, let me emphasize that I have found these cancers of the prostate to be radioresistant. Rarely do we see a case such as the one shown by Dr. Burnam where superficial external irradiation is sufficient to control the growth. It must be supplemented by internal irradiation. If we believe from our cystoscopic examination and palpation that the cancer is roughly confined to the posterior lobe, then there are two methods of treatment: external irradiation and the insertion of radium every two months over a period of six months to control the cancer. If the lateral and median lobes are involved as well as the posterior, then I think the method of election is to do a suprapubic prostatectomy and implant radium in some form into the prostate through the suprapubic opening. It must be remembered that the posterior lobe, which is almost always involved, is far below the bladder neck. That must be watched and treated intraprostatically with radon.

I have not found retention of urine to be relieved by irradiation in any form. I think Dr. Burnam was fortunate in the case he reported which was relieved. If there is retention I think you must decide to do a transurethral prostatectomy and treat the cancer as above outlined.

Let me give the statistics covering a period before we used external irradiation at all. In the first series of 40 cases, 5 cases, or 10 per cent, were well for five years. In the second series of 351 cases (20 per cent too extensive for any treatment), 29, or 8.3 per cent, were controlled for three years and 20, or 5.7 per cent, for five years. Our material I suppose is much like that which Dr. Burnam sees. In 322 fatal cases, 294 were extensive, 19 medium and 9 small.

This slide shows how frequent bone metastases are—44, or 28 per cent, of 156 cases showed bone metastases. At present we use external and internal irradiation and I think we can approach 10 per cent cure.

Dr. Burnam (closing). I am grateful to Dr. Barringer for a kind and illuminating discussion. From a review of our cases here, I am convinced that crossfire irradiation is an important procedure, not only from the standpoint of palliation, but also in properly selected cases from the standpoint of cure. So far as I know the 2 cases which I have reported as cured are the only ones to be found in the literature. It seems to me obvious that there is a wide variation in the radiosensitivity of cancer of the prostate and that a certain percentage of them, if seen early enough, can be cured in this way. I am sorry Dr. Barringer is not here to tell you whether his cured cases were all early cases. I believe these cases were treated by radium implantation or radium needles alone. All of the cases treated by Mudd and his associates apparently have been very advanced.

I am somewhat surprised at the statement of Dr. Barringer that obstruction due to cancer of the prostate has, in his experience, never been relieved by irradiation, and wonder if this is because he has principally resorted to the implantation method. That implantation is a very valuable procedure is beyond question, but I believe this method should be restricted to cases in which the extent of the disease is such that the whole volume can be adequately implanted.

The conclusions I draw are that early cancers of the prostate, where radical operation or implantation is indicated, should first receive a series of crossfire treatment over a period of two to three weeks. This is even more imperative in the borderline cases. In the cases having large growths, except those which respond favorably to external irradiation, it would seem somewhat doubtful if anything could be accomplished by implantation. All cases with obstruction, which do not yield to irradiation, should promptly have conservative surgery. My own impression is that intravesical resection is safer and better than attempts at partial prostatectomy.

SERUM THERAPY IN CANCER*†

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THE chief weapons at present being used in the fight against cancer are surgery, radium and roentgen rays. Success in treatment, however, results only in those cases where the cancerous lesion is in its earliest stages; and because, even in such cases, these methods do not always produce cure, investigations toward finding a more universal remedy are constantly being carried on. Persistent attempts are made in different branches and fields of research to introduce some new and supposedly better method of cancer therapy. The numerous therapeutic agents suggested embrace every field of medicine, physics and chemistry, while quackery of every description has been foisted upon the public as a cancer panacea.

Various investigations have been carried out to explain the many phases of cancer biology. Frequent suggestions have been made, based upon laboratory findings, to alter the life cycle of the cancer cell. Thus, predicated on Warburg's theory of cell respiration, attempts were made to alter this phase of cell life, with no effect, however, on the destructive cancer growth.

The acidosis treatment of cancer suggested by Fischer-Wasels[5] has been proved ineffective by one of us, as well as by others. Hormonal action on animal new growths has been used as a basis for cancer therapy, but, following a short period of mistaken enthusiasm, such methods of treatment have proved fallacious and of little value.

We shall not catalogue here all the attempts, methods, remedies, quackeries, etc., that have appeared, and still appear continually in the literature; we shall confine ourselves to presenting the plan of our present investigations and the results thus far achieved.

Regardless of the differing viewpoints as to whether cancer is a local or a general disease, the cancer patient must be regarded as a very sick person. Any treatment, therefore, should not be limited to the local tumor manifestation but should also take into consideration the entire human being. In other words, we must direct our attack on cancer in two directions: (*a*) to the cancer cell as a spreader of the disease, and (*b*) to increasing the resistance of the tumor bearer.

With these objectives in mind, we formulated the following plan of procedure:

(1) To transfer blood serum from entirely healthy human beings to individuals suffering from cancer.

(2) To prepare a supposedly "antigenic" serum; i.e., a counteracting serum, in animals, for human cancer.

(3) To prepare a control comparable with serum, item (2).

Following is the theoretical basis of our experimental work: Freund and Kaminer[6] showed that the blood serum from healthy human beings is able to dissolve human malignant cells, while blood serum from those suffering from cancer fails to do so. Many investigators, as well as one of us,[7] have further shown that various chemical compounds in the blood of patients with advanced cancer differ quantitatively from those in the blood of healthy human beings. Whether or not the different values of the chemical compounds in the blood stream are primary or secondary factors of the cancer disease, we cannot fail to consider the fact that the blood compounds from cancer cases differ from the normal ones in their values, some being higher, and some lower. Logically, our aim and procedure were to restore the blood stream of the diseased patient to normal balance since the

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blood stream is the most important biological fluid in the human body, supplying nourishment to the cells and to the organism as a whole. This is also a necessary procedure even in cases where the tumor mass has been made to disappear by roentgen rays or radium (in other words, has been absorbed), because the destroyed tumor substance may influence the whole body and upset the normal and constant balance of the blood stream. In many cases among animal transplantable tumors, it was observed that after we had succeeded by various means in making the tumor disappear, the animal later died, not from the cancer but from the absorption of the toxic tumor. For this reason we regarded it advisable to introduce normal blood serum, as much as possible, into cases treated by roentgen rays, radium or surgery, in order to restore the blood stream to a normal balance, and at the same time, as already stated, to dissolve whatever cancer cells may have remained after irradiation, thereby preventing recurrence.

It has been established that growth is a function of cells which can be stimulated or controlled, and by doing this, we help the diseased organism to return to normal equilibrium and increase the patient's resistance. Abderhalden speaks of a special inhibitory ferment in the blood of healthy human beings, the "Abwehrfermente." Freund and Kaminer have also demonstrated such "Abwehrstoffe" in the blood of normal human beings, which, however, was not present in those suffering from cancer. Based also on the above-mentioned observations we found justification for our plan of injecting normal human blood serum into patients suffering from cancer.

Our second task concerned itself with the problem of the possibility, through transferring human blood from cancerous or sarcomatous individuals to animals, of developing a counteracting or so-called "antigenic" serum.

The etiology of malignant tumors is still unknown; whether the real cause of malignant tumors is in the form of a living organism, an enzyme, or a chemical compound—the last word has not yet been said; but, whatever the cause, the results are the same. We know that cancer is an uncontrolled growth, which, in most cases, eventually affects the whole organism and results in death. Of one thing, however, we can be sure, namely, that something must exist or be formed in the human body, which gives rise to spontaneous malignant growth. We know that endogenous and exogenous factors play a great rôle in tumor formation. There is no longer any doubt that malignant growth can be produced by various kinds of irritation, either chemical, physical, or thermal, such as tar, arsenic, roentgen rays, ultraviolet rays, burns, etc. Moreover, something may exist or be formed in the human body as a product of the metabolism itself such as indol, lactic acid, estrogenic compounds, etc., which can produce irritation and be regarded as an endogenous factor.

We may therefore say that by different means the normal cell can be changed into a malignant one and not necessarily by only one specific substance. It may be a chemical, physical or biological factor capable of changing the metabolism of the normal cell and making it different so as to form subsequently an undifferentiated growth. This growth, beginning as a local manifestation, sooner or later involves the whole organism.

We know that malignant cells are short-lived, and that the dead cell must eventually reach the blood stream. Caspari[3,4,6] called these destroyed particles from the cancer tissue "necrohormones," because they originated from the necrotic part of the tumor. In the problem of cancer we cannot speak in terms of specific antibodies as in immunology, since a specific immune serum reacts only upon biologically similar substances; thus, tetanus antitoxin reacts only upon toxin produced from the tetanus bacillus, etc. As already stated, cancer-producing substances may be found among various agents or products of the metabolism itself. It is not unreasonable therefore

to assume that such substances can also exist or be formed within the organism itself which may change the malignant cell back to normal, or in other words, change the organism predisposed to malignant growth, to a resistant one.

We seek also an answer to the question which so often arises as to whether a certain microorganism exists which causes malignant growth. For example, Besredka and Gross[1] recently isolated a microorganism from the blood of mice and fowls several hours after they had been injected with tumor cells. The authors claimed that this microorganism was the real cause of the malignant growth.

Von Brehmer[2] claimed, on the basis of his work, that the microorganism which gives rise to malignant growth is attached to the red blood cells. Based on these theories we undertook the experiment of introducing blood from cancerous and sarcomatous human beings into sheep, and, after a certain period of time, using the serum from the injected sheep for our experiments.

In order to have a control serum for comparison with the antigenic serum, we transferred blood from apparently cured cancer cases (cured by surgery, roentgen rays and radium) which did not manifest any signs of recurrence after one, two or more years. We also injected sheep with blood from entirely healthy human beings —those in whom there was no change in general metabolism, nor any other disease—in order to have a control for the new type of serum which was obtained from mixing the blood of the different species, human and animal.

PROCEDURE AND METHODS

As above stated, our starting point in this serum therapy was the transfer of serum from normal, healthy human beings to cancer patients. For the former we chose individuals who had suffered some accidental injury, or had high blood pressure. The blood was taken from the arm veins by means of a syringe, placed in tubes and centrifuged. Later, under highly aseptic precautions the serum was decanted with a capillary pipette and placed in another sterile tube. Then the serum was injected directly into the patient. At times, the serum was inactivated at 56°C. for thirty minutes before injection. This procedure was usually employed in the instances where it was not possible to inject the prepared serum into the cancer patient directly after the blood was taken.

The quantity of serum injected at any one treatment was dependent upon the amount of blood we could take from the healthy individual. Usually, we tried to get the largest possible amount. The dose of serum used for one treatment was from 30 to 40 cc. Injection was usually given in the buttocks. This region was chosen as being the most convenient and appropriate site because of the large muscle available to absorb a quantity of injected fluid. Sometimes a portion of the serum was, when possible, injected near the tumor.

In our opinion the transfer of serum from one person to another was far more convenient than blood would have been because (*a*) it was not necessary to test the blood grouping as in blood transfusions, and therefore we could use any available case in generally good condition, or cases with high blood pressure; (*b*) we could inject serum more often than blood—usually two to three times a week, 30 to 40 cc. of serum per injection. In transferring serum from one person to another, we never observed any anaphylactic or foreign body reactions, such as changes of temperature, or the presence of albumin in the urine; nor any local swellings or necrosis from injection of the large amount of fluid. On the contrary, the serum was absorbed without any untoward effects.

The results so far achieved, using the above-described procedure and treatment, are satisfactory. The general condition of the patients thus treated for a longer period of time with normal human serum in most instances was improved, i.e. some of the patients gained weight and felt generally

better. With regard to specific effects of the normal serum treatment on the local tumor, we cannot express any definite conclusion, although we have observed some definite regression of the tumor in certain cases.

Although we are fortunate in being connected with one of the largest hospitals in the world, our work is delayed because of lack of suitable patients from whom the desired amount of blood for cancer cases may be drawn. Based on our observations in several cases, we can recommend this serum treatment, not, of course, as a direct specific cure for cancer, but as an additional procedure with other therapeutic methods, because, in all cases, the general condition of the patients so treated has greatly improved.

Due to the great difficulty in finding suitable persons from whom to draw sufficient blood for use in treating cancer patients, the thought occurred to us of finding another medium, more universal and less expensive to use. Accordingly, we chose sheep for our work because, as spontaneous tumors are not known to occur in sheep as they do among other animals, it may be assumed that the sheep has some resistance against cancer; moreover, the work of Lumsden and Kohn-Speyer[9] has shown this animal appropriate for such experiments.

Our method of procedure was then as follows: Blood was taken from cancerous, sarcomatous patients, and other persons, as already outlined. The blood, defibrinated with glass beads, was injected into the sheep (partly intravenously and partly intramuscularly) in specific doses and intervals of time, in accordance with the behavior and reactions of the sheep. Details regarding this technical procedure will be published in a separate article.

After about three months the blood from the sheep thus injected was drawn, and a serum prepared.

Before describing the use of this experimental sheep serum for human beings, we desire to refer to our experiments carried out on cultures of human tissues in vitro. We were most anxious to find out how this experimental sheep serum reacted on growth of human tissues in vitro as compared with serum from entirely normal sheep, before employing it in human beings. We used the sheep serum as a part of the medium necessary for tissue cultures in vitro. The procedure employed in these tissue culture studies was published in complete detail in a separate communication.[8] We shall mention briefly here the results observed, which we regard as very interesting phenomena.

For the tissue culture study, human tissues from normal human thyroid and carcinoma of the breast were used. As a part of the medium, normal sheep serum and experimental sheep serum were added. The following observations were made:

The above-mentioned human tissues grew excellently in the medium when normal sheep serum was added; no growth was observed when treated sheep serum was added. Through further experimentation we observed that this experimental sheep serum is not toxic to living cells, i.e. it will not kill the cells, even if they are left in the medium for several days. It will only inhibit growth. For example, when cultures of living human tissue were left in a medium containing a certain amount of experimental sheep serum, no growth was observed. However, when the same cultures were washed and separated from the old medium, and placed in a fresh medium containing normal sheep serum, the tissue started to grow. Another striking phenomenon observed was that fragments of embryo chick heart placed in a culture medium containing a portion of the treated sheep serum, although they produced no proliferating cells in its presence, still continued to beat. Normal proliferation of these chick heart fragments took place upon transfer to normal medium. Because of these observations we felt justified in trying this treated sheep serum on tumor-bearing patients.

As no method exists for determining the

dosage of sheep serum that a human organism can tolerate without developing anaphylactic disturbances, we had, first of all, to devise a method of using this serum. We knew that we would have to take into consideration anaphylactic reactions which might arise through the introduction of foreign bodies into a human organism. Several months were therefore required to ascertain the appropriate method of using the experimental sheep serum for cancerous patients.

The Welfare Island Cancer Hospital offered us the opportunity of observing patients over a long period of time. This was a most important and fortunate factor in carrying on such experimental procedures as we required. We have been using this experimental sheep serum for several months without any danger of anaphylactic reactions, or serum sickness.

The experimental sheep serum was injected, partly intravenously and partly intramuscularly, into the buttocks and near the tumor lesion, the patient being previously desensitized by the injection of a very small amount of serum. Usually we started with 1 cc. of the experimental sheep serum, increasing the dose in the subsequent injections. It should be mentioned that the tolerated dose of serum must be found for each individual case. Some of the cases treated could stand injections up to 30–40 cc. of the experimental sheep serum without demonstrating any symptom of anaphylactic reaction, whereas others developed chills or showed a rise in temperature following injections of 10 cc. of serum. In such cases smaller doses were administered in further treatments, with subsequent moderate increases.

We used this experimental sheep serum for inoperable cancer patients who did not react to roentgen or radium therapy, in order to discover, first, the specific reaction of the tumor growth to the serum. The serum was also used in combination with roentgen and radium therapy as we assumed that the serum would make the cancerous cell more sensitive to irradiation, or the organism more resistant to the malignant disease.

In our further experiments using the tissue culture method we have observed that the experimental sheep serum exerted a definite inhibition upon cell proliferation of human tumors grown in vitro, where it was added to the culture medium in the proportion of 1:3. However, it was further noted that the inhibitory effect of this serum was lessened as the serum was more diluted. We have also observed that the growth inhibitory substance is contained in the proteins of the serum.

Consequently our aim is to isolate this specific protein fraction which exerts the inhibitory action upon the cell proliferation. In this way it may be possible to increase the effectiveness of the experimental serum.

It should be noted here that serum from sheep which had been treated with normal human blood for control studies had no inhibiting effect upon human tissues grown in vitro, both normal and malignant. We hope that further studies with this experimental sheep serum will throw more light on this problem. As the results of our experiments we have succeeded in developing a serum by means of transferring blood from human advanced cancerous patients to sheep. This serum possesses a definite inhibitory action upon cell proliferation in vitro without exerting any toxic effect on the organism.

In the meantime, we feel that the use of this serum has been beneficial, and while it is not a definite specific agent in the control of cancer, we have noted that as an additional form of therapy it enhances the effect of roentgen and radium irradiation, which is given in conjunction with it.

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THERAPEUTIC USES OF ESTRIN*

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RECENT developments in the therapeutic uses of estrin include an increase in the number of estrogenic compounds available for clinical use, an increasing number of applications to various clinical conditions, the employment of higher doses, and the demonstration in animals of the possible carcinogenic action of these compounds when administered in great quantities over long periods.

The majority of the established or proposed therapeutic uses of estrin are of interest to radiologists since conditions involving the pituitary, ovary, uterus, breast and prostate have been combated by a variety of radiological procedures. Moreover the recent reports suggesting a relationship between estrin and cancer involve a major sphere of interest for irradiation practice.

Before discussing in detail any form of estrin therapy it is necessary to clarify, if possible, the confusion regarding the various forms of estrin, the units of dosage, and the relationship of the estrogenic hormones available for therapeutic use to natural ovarian secretions. There are two groups of estrogenic hormones available for clinical use, one for administration intramuscularly, and the other for administration orally. Amniotin (Squibb) and theelin (Parke-Davis) are trade names for ketohydroxyestrin. This is the form of estrin on which the international unit is based and it has been obtained in crystalline form from the secretions of the ovarian follicle. Progynon B (Schering) is a trade name for benzoic acid ester of dihydroestrin. This modification of dihydroestrin by the addition of phenolic hydroxyl was made to prolong its physiological effect. These estrogenic substances for intramuscular use may also be given by mouth but are less active. Theelol (Parke-Davis) is trihydroxyestrin and although less potent than the other forms of estrin, is supposedly more active by mouth. Progynon D-H (Schering) is prepared for oral administration and is dihydroestrin. Emmenin (Ayerst, McKenna and Harrison) is prepared from the placenta for oral use and is believed to decompose in the body to trihydroxyestrin.

In the past, the doses of estrogenic substance have been expressed in terms of mouse units, rat units, gamma, and international units, none of which have corresponding values. It is preferable to express the dosage in terms of international units. It is convenient to remember that 1 milligram of ketohydroxyestrin is equivalent to 10,000 international units, a dose which is available on the market and a convenient one for clinical use. Since the action of drugs is proportional to the body weight, the ratio of the weight of the material administered to the body weight should be kept in mind in attempting to deduce clinical applications from results obtained in animal experimentation.

One milligram of estrin, an average clinical dose, is equivalent to 1/60,000,000 of the weight of an average person, and the dosage is usually continued over a period of several months. In animal experimentation on the carcinogenic action of estrin the dose administered is often as high as 1/100,000 of the body weight and it is continued over the greater part of the lifetime of the animal.

CLINICAL USES OF ESTRIN

The clinical uses of estrin depend upon three major physiological actions: (1)

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stimulation of the growth of uterine epithelium and musculature and a maturation effect on the squamous epithelium of the cervix and vagina; (2) stimulation of the growth of ducts and periductal tissue in the breast; (3) a depressant action on the function of the anterior pituitary gland. In general, the effect on the prostate resembles that on the uterus.

Gonorrheal Vaginitis. Lewis reported on the treatment with estrin of gonorrheal vulvovaginitis in children in 1933. The favorable results of this method of therapy, which have been confirmed by others, are dependent upon the maturation of squamous epithelium in the vagina and cervix. While many of the cases respond within a few weeks or a month, the therapy must be prolonged in some instances. The details of the treatment will not be discussed here since they are not of particular interest to radiologists. Apparently this use of estrin has a permanent place in clinical medicine. Other proposed uses of estrin which will not be detailed here since they have not been clinically established are: its use in hemophilia, in arthritis at the menopause, in migraine, and in hypertrophy of the prostate. The changes produced by estrin may increase urinary obstruction in prostatic hypertrophy. This use of estrin as well as attempts to bring about abortion or increase in the libido is not founded upon fact.

Manopausal Symptoms. At the present time estrin has its greatest therapeutic application in attempts to modify the menstrual cycle. In this field, treatment is still handicapped by a lack of knowledge concerning the normal physiology of menstruation. Its most widespread clinical use is for menopausal symptoms. In this condition estrin therapy is substitutive, although certain observers believe that it may act as a depressant of the anterior pituitary gland. The vasomotor disturbances of the climacteric along with mild psychic changes can usually be controlled by the oral administration of estrin. Hot flashes followed by a feeling of chill and accompanied by insomnia may be treated with amniotin capsules, theelol, progynon D-H, or emmenin administered daily by mouth. The dosage varies from 1/10 mg. to 9/10 mg. daily according to the type of preparation used.

Novak has discussed the value of this therapy. Reports have been contributed by Severinghaus and by Mazer and Israel. A recent report has been made by Everett. For severe symptoms such as mental depression, precordial discomfort, palpitation, dizziness, nausea, paresthesia, vertigo and sweating, intramuscular injections are necessary; 10,000 to 50,000 international units (1 to 5 mg.) given twice weekly for a period of three weeks will usually combat the severe symptoms. Mazer and Israel found that 50,000 international units every fourth day was necessary to treat involutional melancholia. These doses were gradually reduced after the fifth or sixth injection. Treatment should be prolonged for from two to six months. In some cases treatment must be prolonged beyond this period.

Certain investigators have claimed that the effects of estrin therapy in the menopause can be measured by suppression of prolan in the urine. This is apparently in line with the thought of those radiologists who have treated menopausal symptoms by irradiation of the pituitary. However, the author in conjunction with the Squibb Biological Laboratories has tested urine for prolan in over 300 cases of women beyond the menopause and we find no correlation between menopausal symptoms and the presence of this substance in the urine. Mazer and Israel are of the opinion that the therapy is largely substitutive. The mode of action of the estrin in these cases, however, remains to be established.

Acquired Ovarian Deficiency. Symptoms of ovarian deficiency similar to the natural menopause may follow castration by surgery or irradiation. In such cases the symptoms usually follow about six months after castration.

According to most observers the natural menopause has its onset at an average age

of approximately forty-one, although the menses do not cease until the ages from forty-five to fifty in 70 per cent of normal women. At this time thickening of the ovarian capsule is accompanied by or inhibits rupture of the ovarian follicle so that the corpus luteum fails to form. This inhibition of one of the endocrine functions of the ovary is accompanied by increased activity of the anterior pituitary which may lead to a mild degree of hyperthyroidism, emotional instability, and changes in the mammary tissue. A similar ovarian deficiency may be acquired earlier in life as a result of inflammatory changes in the tubes and ovaries following gonorrheal infection. Nausea and vomiting acquired during the stage of active pelvic peritonitis may persist as a symptom secondary to the ovarian deficiency long after the subsidence of the inflammatory changes. In these cases of acquired ovarian deficiency, moderately high doses of estrin (10,000 international units once or twice weekly for a period of several months) are valuable adjuncts to treatment. In some of these cases the mammary changes are the outstanding feature and they have been classified as mazoplasia or an early stage of chronic cystic mastitis.

Chronic Cystic Mastitis. Endocrine therapy in chronic cystic mastitis has been discussed in a forthcoming contribution (Lewis and Geschickter). The use of estrin in cystic mastitis has been reported by Dahl-Iversen and by Mazer. Estrin is most successful in the early stage of chronic cystic mastitis, characterized by premenstrual pain or by mammary pain of longer duration accompanied by tender tissue in the upper and outer quadrants of the breast which palpates as a flat granular area of increased density. This early stage of chronic cystic mastitis responds to estrin administered intramuscularly twice weekly in doses of 10,000 international units. The doses are not given during menstruation and after two months are gradually tapered off, so that the third month one injection a week, the next month only two injections and finally only one injection a month at the premenstrum is given, administering 10,000 international units at each injection.

The same method of estrin therapy can also be employed successfully for the proliferative stage of chronic cystic mastitis, known as adenosis or Schimmelbusch's disease. This phase of the disease is characterized by menstrual disturbances, loss of weight, apprehension (usually a fear of cancer), mammary pain, and a tendency to hyperthryoidism. The breasts are smaller than normal, have a diffuse shotty feeling due to multiple indefinite lumps and they have a definite saucer-like edge. Pain in the premenstrum or throughout the period may be present. This condition usually responds to the same type of treatment recommended for the early phase of chronic cystic mastitis, although the lumpiness of the breast may not entirely disappear. Adenosis tends to recur eighteen months to two years following the course of estrin therapy.

In the form of chronic cystic mastitis characterized by one or more large blue dome cysts, large doses of estrin, 10,000 to 20,000 international units, given twice weekly over a period of several months have occasionally been effective. In other cases, particularly multiple blue dome cysts in younger women, the condition is not benefited and in one case of a woman approaching the menopause who had a cluster of small cysts following the removal of two previous cysts, estrin therapy caused the cystic mass to grow.

Other Conditions of the Mammary Gland. Dilated ducts beneath the nipple with retained mammary secretion may be successfully treated with estrin therapy, using the dosage recommended for cystic disease. In cases of bleeding of the nipple in which no definite tumor can be palpated in the breast, similar doses of estrin may be used in an attempt to stop the discharge. Such cases should be carefully watched and palpated for the development of a tumor. The discovery of such a tumor demands

surgical exploration. In our opinion intracystic papilloma with bleeding should be treated surgically and not by endocrine therapy.

Menstrual Disorders. Estrin has been recommended for the treatment of various menstrual disorders. To date its use in amenorrhea is the only successful application to this group of conditions. There are two drawbacks to the use of estrin in amenorrhea. In the first place estrin does not stimulate the ovary and it may repress the pituitary upon which the ovary is dependent for its stimulation. In the second place, while large doses of estrin and its withdrawal may bring about uterine bleeding, such a reaction is far from duplicating the normal physiological cycle of events in the ovary or uterus. It is unwise to employ this method of therapy without a thorough determination of the cause of amenorrhea, and certainly its use in young girls at the ages of fourteen, fifteen or sixteen should be delayed until normal menstruation has been awaited for an adequate period. Kurzrok, Wilson and Cassiday have reported on the treatment of amenorrhea with large doses of estrogenic hormone.

Estrin therapy in amenorrhea is best combined with other forms of endocrine substance. Ten thousand international units administered weekly for a period of one month may be followed by injections of progesterone, the corpus luteum hormone, in doses of from 1 to 5 rabbit units daily for one week. Werner and Collier, Mishell, and others, have shown that such therapy in the human builds up the normal premenstrual endometrium. In our own experience we have found it useful to follow a course of estrin therapy with injections of menopausal urine hormone (gamone, Squibb). The use of gamone in primary amenorrhea associated with hypogenitalism has been successful in several cases.

The use of estrin in functional uterine bleeding is ill advised. The bleeding may be postponed just as a menstrual period can be suppressed or delayed with large doses of estrin, but such results are only temporary. Other endocrine preparations such as progesterone (proluton, Schering) are more effective. Progesterone is also more valuable in cases of dysmenorrhea or mid-period pain (Mittelschmerz).

Pituitary Disorders. It has now been definitely demonstrated that large doses of estrin interfere with normal pituitary function. Hypopituitism with pituitary adenomas have been produced by Cramer and Horning and by Zondek, in rats following high doses of estrin. Suppression of the pituitary apparently without pituitary damage can be accomplished by the administration of 20 to 50,000 international units of estrin in the human, the injections being given every fourth day. I have utilized this depressant action on the anterior pituitary in the treatment of galactorrhea, and diabetes insipidus which did not respond to pituitrin. In cases with inverted or absent nipples where childbirth is followed by mammary swelling, pain and abscess, this therapy can also be used for the suppression of lactation. It is well to point out that this suppression of the pituitary in response to estrin may wear off after a period of months. In these cases progesterone can be utilized thereafter to suppress pituitary activity. It is possible there are other uses in endocrinology for this depressant action of estrin and progesterone on the pituitary, and it is well to consider this form of therapy before administering radiation therapy to the pituitary gland.

Relation of Estrin to Cancer. Lacassagne induced carcinoma of the breast in male mice with injections of estrin in strains in which the females were normally susceptible. Gardner, Smith, Strong and Allen reported the development of sarcoma in 5 male mice receiving estrogenic hormones. Loeb and his collaborators observed 6 cases of sarcoma in mice. Because of these experiments, estrin therapy is looked upon by some as increasing the probabilities of cancer in patients. Such an interpretation of these experiments seems illogical since it fails to evaluate the factor of dosage. In

Lacassagne's experiments estrin in amounts approximating 1/200,000 of the body weight of the mouse was administered at a single dose and the dose was repeated weekly throughout the life of the animal. A corresponding dosage in a patient weighing 60 kilograms would necessitate the administration of 0.3 gram of crystalline estrin at a single dose and the injections would have to be begun in early childhood and continued throughout life. The estrin therapy herein advised is well below the amounts present in normal pregnancy. Cramer and Horning, in discussing the induction of cancer in mice with estrin stated that "the carcinogenic changes here described were produced by the administration of estrin prolonged over a period representing a considerable fraction of the normal span of life of a mouse and corresponding in man to a period of from 7 to 10 years, while the therapeutic administration of oestrin preparations in man is, in skilled hands, limited to short periods of a few weeks or months. The development of mammary cancer described in this paper should not, therefore, be used as an argument against the therapeutic application of oestrin preparations."

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MASSIVE ROENTGEN IRRADIATION OF THE HYPOPHYSIS IN EXPERIMENTAL DIABETES

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THERE is apparently sufficient clinical evidence[7,16,18,21] to support the theory that irradiation of the pituitary gland exerts a synergistic effect on carbohydrate metabolism in patients with diabetes. It was the object in this bit of experimental work to determine if the pituitary gland alone, after removal of the pancreas in animals could be induced by massive doses of roentgen rays to influence this metabolic process.

The universal conception of the primary cause of diabetes is lack of endocrine secretion (insulin) from the pancreas which disturbs sugar metabolism. That other etiological factors may be present is suggested by: (*a*) failure to find typical and constant lesions exclusively characteristic of the disease in many, if not most, fatal cases of diabetes,[1,5,19] (*b*) the observation that 90 per cent of the pancreas must be removed or destroyed in experimental animals before severe symptoms of diabetes are produced;[23] (*c*) that extracts of the pancreas in fatal cases have shown insulin to be present in amounts that would maintain life for several weeks.[10] The secretion from the adrenal gland undoubtedly exerts some influence on carbohydrate metabolism in diabetics. Gordon[16] cites numerous instances where irradiation produces marked changes in blood sugar, small doses increasing blood sugar while large doses decrease its volume.

Undoubtedly there are sufficient clinical and experimental data to warrant careful clinical and exhaustive research into the true effects of the influence of irradiation on the pituitary gland in diabetes, both clinical and experimental.

Whether the control of diabetes is centered in the pituitary, diencephalon, tubero-infundibular region or a combination of any part or all of the surrounding vegetative nervous system cannot be determined at this time. A careful review of the effect of irradiation on this area in an effort to control diabetes is very discouraging. Practically all of the work is empirical, particularly in clinical cases. In most instances the dosage is grossly indefinite, so much so that one is usually at a loss to know not only the surface dosage in any term, but as a rule one cannot even know what type of rays were used in treating the patients.

As early as 1884, Loeb[22] observed the occurrence of diabetes in some cases of acromegaly. Pierre Marie confirmed this observation several years later (1886), and since then Borchardt,[4] Davidoff and Cushing,[9] Rowntree,[24] and others, have reported coincidental diabetes in 25 per cent or more of their cases. Davidoff and Cushing, viewing their clinical and anatomical observations in acromegaly, believe that the coexistent diabetes is due to hyperfunction of the acidophil cells of the anterior lobe. That the basophil cells may also exert a diabetogenic action is indicated by the observations of Cushing,[7] who found hyperglycemia and glycosuria in cases of pituitary basophilism. Partial extirpation of the adenomatous anterior lobe diminishes the hyperglycemia in most of these cases and increases the tolerance for glucose. Clinical observations have likewise indicated that deficiency of the hypophysis (hypopituitarism) is usually accompanied by an increase in glucose tolerance.

Goetsch, Cushing and Jacobson[15] (1911) were the first to observe experimentally that hypophysectomized dogs have an increased tolerance for glucose. Recently, Houssay[17] and his associates in South

America have reported detailed investigations on the effect of hypophysectomy in both normal and depancreatized animals. These workers find that in normal animals the removal of the hypophysis leads to: (1) a low fasting blood sugar which reaches convulsing levels during fasting; (2) a marked sensitivity to insulin which produces fatal convulsions in doses as small as 0.5 units per kilo, and (3) an increased tolerance to both ingested and injected glucose. These observations have been amply confirmed by Geiling and Britton,[13,14] Corkill, Marks and White,[6] and others.

In completely depancreatized dogs in which the symptoms of diabetes are severe, hypophysectomy greatly diminishes the intensity of the disease and prolongs the life of the animal. Thus hypophysectomized depancreatized dogs survive for eight months or more, while depancreatized controls not receiving insulin succumb within one or two weeks. In these animals hyperglycemia, glycosuria, azoturia, ketonuria and polyuria are decreased; the tolerance for glucose is increased; the respiratory quotient, which is low during fasting (0.64–0.75), is raised indicating that glucose is utilized in these animals. Most of these findings have been confirmed by Barnes and Regan,[3] Soskin,[25] and Kutz et al.[20]

Converse changes to those noted after hypophysectomy are brought about by the injection of suitable extracts of the anterior lobe into normal animals. Thus Houssay and Biasotti[17] found that hyperglycemia and glycosuria resulted; Bauman and Marine observed lipemia and polyuria; and Anselmino and Hoffmann[2] found acetonemia. Although the exact rôle of the hypophysis in carbohydrate metabolism is still obscure, it appears that the gland secretes a hormone which antagonizes insulin, and which stimulates gluconeogenesis. In doing this, it may act with, or be activated by, other endocrine glands, especially the adrenals and the thyroid.

IRRADIATION OF THE HYPOPHYSIS

Since the hypophysis elaborates a diabetogenic hormone and since its removal reduces the severity of experimental diabetes, it was thought that heavy doses of roentgen rays directed to the gland might produce similar results. A search of the literature revealed that Cushing[7] had treated successfully with roentgen rays a patient with pituitary basophilism showing hyperglycemia (219 mg. per cent) and glycosuria, and requiring 65 units of insulin daily. This patient became entirely sugar-free on an ordinary diet without insulin. The roentgen dosage used is not stated. Hutton has reported successful treatment of hypertension with diabetes by administering small doses (106 r). Three patients were relieved of both conditions; glycosuria disappeared, blood sugar reduced to normal as well as blood pressure. An article by Fucci[12] is of no value to us in attempting to study the effect of roentgen rays, granting that his observations and conclusions are correct, because neither the wave length used, the voltage used, nor the estimated depth dose is mentioned.

METHODS

In our studies 7 dogs were rendered diabetic by complete removal of the pancreas. After recovery from the operation, which usually required about three weeks, the animals were kept on a basic diet of dog biscuits, sugar and ground meat, to which was added liberal amounts of fresh or dried pancreas. On this stock diet 2 units of insulin per kilo of body weight was given twice daily at the time of feeding. Between periods of observation no special attempt was made to control the diabetic condition; the animals were seldom given sufficient insulin to render them sugar-free, yet they were never permitted to show marked glycosuria or ketonuria. Prior to periods when the tolerance to glucose and insulin was determined, the animals were

maintained in an approximately constant diabetic state. For each kilo of body weight the diet consisted of 30 grams of a stock meat preparation (Marco), 5 grams of sugar and 4 grams of fresh pancreas or 1 gram of pancreatin (Parke-Davis). On this diet insulin was given twice daily in doses of 2 units per kilo of body weight. After the animals had been subjected to these standardized conditions for at least two days, food and insulin were withdrawn for a period of twenty hours and tolerance tests were made.

The glucose tolerance tests were carried out in the customary manner: following the taking of an initial blood sample, the animals were given 1.75 grams of glucose per kilo of body weight, and subsequent blood samples were taken at 15, 45, 75 and 105 minutes. The glucose of the blood was determined by the method of Folin.

To test the animal's sensitivity to insulin, food and insulin were withheld for twenty hours during the period of controlled diabetic state. Two to two and one-half units of insulin were then administered and the animal was observed over a period of four hours to see if convulsions occurred.

Following one or more control tolerance tests, the animals were given varying doses of roentgen rays. In order to render the animals immobile during the long treatment, they were anesthetized with nembutal, and tied to a support which held the head securely in any desired position. The rays were delivered to the hypophyseal area through one dorsal and two lateral portals, each 5 cm. square. The physical constants employed were: 140 kv. (mechanical rectification) with 5 ma., a focal skin distance of 50 cm. and 0.5 mm. copper and 1 mm. aluminum filtration. With these constants the Coolidge tube delivered 5.8 r per minute. The total dose given the hypophysis, as calculated by the Bachem tables, varied between 750 and 2,025 r for a single treatment. Four of the animals were given a second and heavier treatment about one month after the first. Subsequent glucose and insulin tolerance tests were carried out at weekly intervals following irradiation.

It is to be remembered that 750 r, and above, delivered to the pituitary are to be considered massive doses. The object was to determine whether destructive irradiation exerted any influence on the glandular control over carbohydrate metabolism. It is our plan to continue this work with smaller doses (100 r and upward) in an effort to determine if the so-called stimulating dose produces any changes in depancreatized animals.

RESULTS

1. *Sugar Tolerance.* The data presented in Table 1 and Charts 1, 11, and 111 show a wide variation in the fasting blood sugar of most of the animals following irradiation. In 2 animals, No. 1 and 5, the sugar level was lower after treatment, suggesting that irradiation might have been beneficial; the nutritive condition, however, of these animals became greatly impaired soon after irradiation, a fact probably accounting for the reduction in blood sugar. In all other animals the fasting sugar level was either unchanged or was actually higher than the initial pre-treatment level as in the case of 3 animals (No. 2, 4 and 6), the blood sugar of which was 75 to 100 mg. higher after irradiation. The course of the blood sugar after ingestion of glucose was the same after treatment as before. The highest value was attained in most animals after forty-five minutes; the concentration decreased thereafter at a rate of about 10 mg. per cent for each succeeding half hour period.

2. *Insulin Sensitivity.* Irradiation did not render the animals hypersensitive to insulin during fasting for convulsions never occurred in any of the animals given 2 units per kilo, and all animals but one (No. 5) tolerated 2.5 units per kilo.

3. *Glycosuria.* That glycosuria was not greatly reduced by irradiation was indicated by the fact that the 2 heaviest irradiated animals eliminated glucose in amount

TABLE I

GLUCOSE TOLERANCE TESTS OF DEPANCREATIZED DOGS BEFORE AND AFTER IRRADIATION OF THE HYPOPHYSIS

	Dog. No. 1	Dog. No. 2	Dog No. 3	Dog No. 4	Dog. No. 5	Dog. No. 6	Dog. No. 7
Depancreatized	10/8/33	1/1/34	11/22/33	1/2/34	12/12/33	3/2/34	3/24/34
GLUCOSE TOLERANCE BEFORE IRRADIATION							
Mg. per cent glucose at 0, 15, 45, 75, 105 min.	498,574,606 606,613	370,418,459 462,465	186,241,305 367,357	236,303,385 394,400	207,285,377 364,316	346,400,432 439,428	319,343,412 408,396
First irradiation	1/2/34	1/24/34	1/13/34	2/5/34	2/12/34	3/15/34	4/6, 7, 9/34
Dose to skin per portal	500 r	500 r	650 r	700 r	1,000 r	1,350 r	1,350 r
Dose to hypophysis	750 r	900 r	975 r	945 r	1,500 r	1,820 r	2,025 r
GLUCOSE TOLERANCE AFTER FIRST IRRADIATION							
1 week				400,465,500 506,485		374,402,436 444,437	381,423,491 485,470
2 weeks	377,423,432 432,430				170,204,269 287,296	471,500,585 562,541	
3 weeks	354,392,465 449,432	446,458,518 540,505	244,280,388 439,400	398,444,602 588,577	188,266,351 345,328	426,526,540 537,533	372,414,454 452,430
4 weeks						479,506,533 563,548	394,437,465 468,457
Second irradiation		2/16/34	2/9/34	2/26/34		4/13/34	
Dose to skin per portal		810 r	780 r	900 r		1,300 r	
Dose to hypophysis		1,460 r	1,070 r	1,220 r		1,750 r	
GLUCOSE TOLERANCE AFTER SECOND IRRADIATION							
2 weeks		555,588,658 694,641	265,315,408 471,436	361,433,480 492,508		444,497,533 537,520	
3 weeks		366,390,423 430,427		341,343,383 426,442		437,485,537 551,523	
4 weeks				333,350,422 464,458		444,506,552 540,536	

nearly maximal for starving depancreatized animals. Thus, dogs No. 6 and 7 excreted 3.2 and 4.4 grams per kilo daily, respectively.

4. *Histological Changes Produced by Irradiation.* The histological studies made on 6 of the 7 animals irradiated indicate that the hypophysis was seriously damaged by the treatment (Table II). In dogs No. 4, 5, 6 and 7 the gland was impaired, as indicated by edema and degeneration of the cells of the pars tuberalis. The nerve structures of the brain, however, showed more clearly the effects of the massive irradiation. Thus, the cortex of all animals and the midbrain of those animals receiving 1,500 r or more of radiation were definitely damaged.

DISCUSSION

It is difficult to explain this almost complete failure to decrease the severity of symptoms of diabetes with definitely proved facts regarding the hypophyseal-islet interrelationship. It may be feasible that in the absence of complete destruction by irradiation the same as in incomplete surgical removal[9] sufficient hormone-producing tissue remains. The amount of destruction of the pituitary necessary cannot be done by roentgen irradiation that is done surgically. In our cases severe damage to the surrounding brain tissue occurred; that is more than could possibly be delivered to clinical cases.

If it is true that irradiation has a beneficial effect, as indicated by different au-

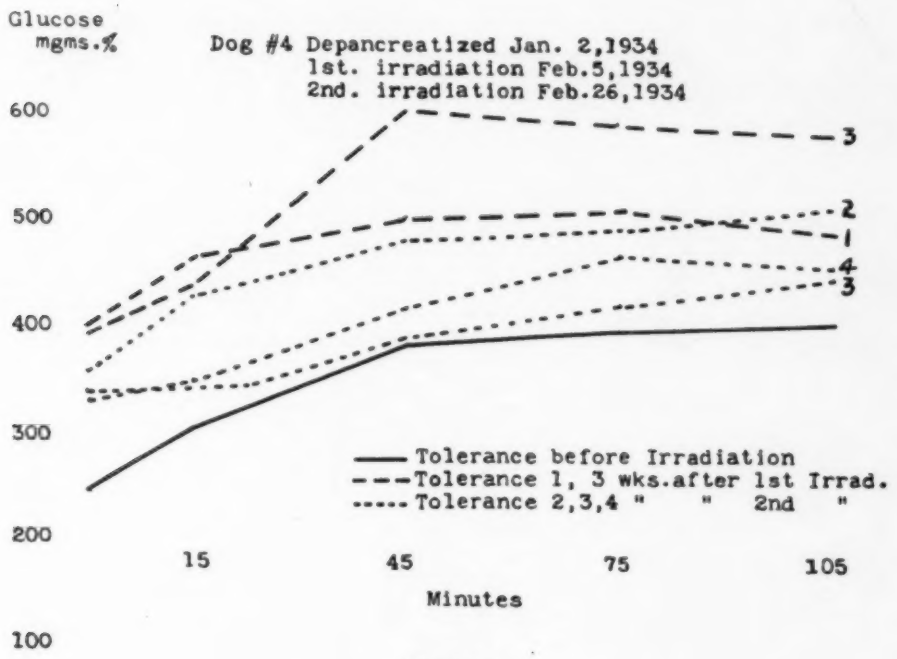

CHART I

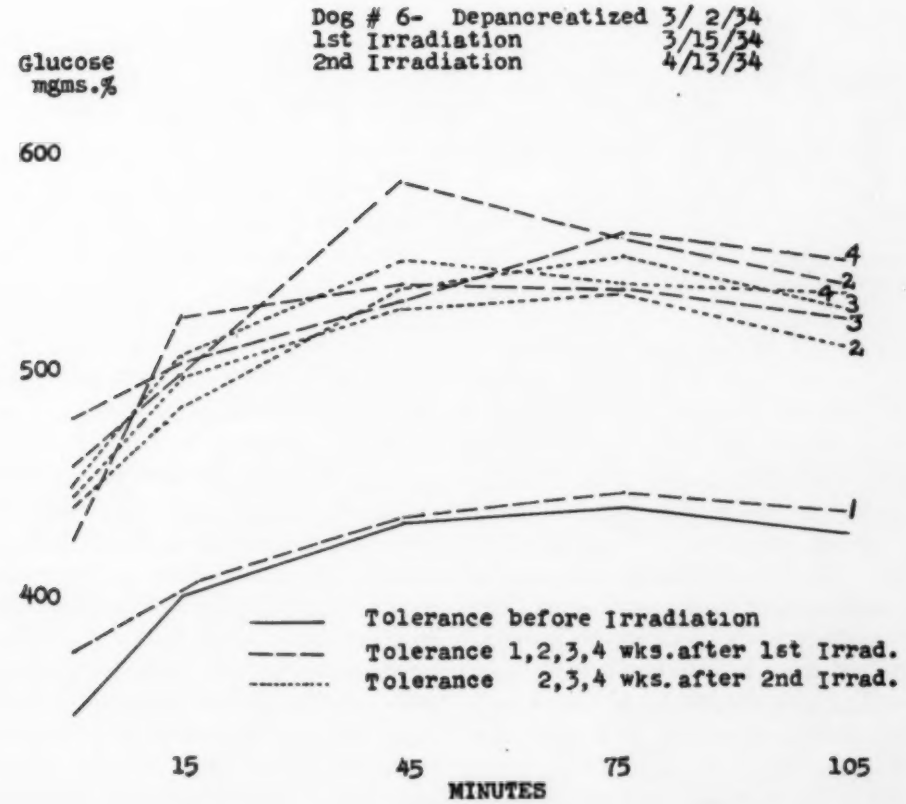

CHART II

TABLE II

SUMMARY OF HISTOLOGICAL STUDIES

	Dog No. 2	Dog No. 3	Dog. No. 4	Dog. No. 5	Dog. No. 6	Dog No. 7
Depancreatized	1/1/34	11/22/33	1/2/34	12/12/33	3/2/34	3/24/34
Killed	3/11/34	2/6/34	3/26/34	3/11/34	6/6/34	5/3/34
Duration of diabetic state	10 weeks	13 weeks	13 weeks	13 weeks	11 weeks	6 weeks
First dose to hypophysis Second dose to hypophysis	900 r 1,460 r	975 r 1,070 r	945 r 1,220 r	1,500 r	1,350 r 1,820 r	2,025 r
Autopsy after irradiation	6½ weeks	7½ weeks	8 weeks	4 weeks	9 weeks	4 weeks
Liver	Fatty degeneration Necrosis	Fatty degeneration Necrosis	Fatty degeneration Necrosis	Fatty degeneration	Fatty degeneration	Fatty degeneration
Ovary	Normal			Sclerotic		Hyperplasia germinal epithelium. Many follicles
Testis		Normal	Tubules degeneration			
Adrenals	Slight congestion	Normal	Cortex and medulla moderate degeneration	Cortex normal. Medulla slight degeneration		Cortex slight degeneration. Medulla normal
Thyroid	Normal	Normal	Atrophied	Normal	Atrophied	Proliferation of cells
Cortex	Congestion Degeneration	Moderate degeneration	Marked degeneration	Marked degeneration	Marked degeneration	Marked degeneration
Midbrain		Normal	Normal	Slight degeneration	Slight degeneration	Marked degeneration
Hypophysis 1 pars nervosa		Normal	Congestion Slight degeneration	Normal	Congestion Slight degeneration	Normal
2 pars intermedia		Normal	Slight degeneration	Normal	Slight degeneration	Normal
3 pars tuberalis		Acidophil cells numerous		Slight congestion and degeneration	Slight congestion and degeneration	Slight congestion and degeneration

thors, then some systematic work should be done to determine the dosage necessary to bring about this end. Experimental diabetes and clinical diabetes are essentially not analogous conditions. There is not a complete pancreatic deficiency in diabetes mellitus and in all probability no hyperfunctioning anterior lobe, presumed to be present in diabetes mellitus, in the depancreatized dog.

Since the physiological state of the depancreatized dog may not simulate the clinical condition, our conclusions do not in any manner deny the reports of improvement and cure of clinical cases of diabetes by irradiation of the hypophyseal area. It is conceivable that in the disease irradiation of the area by doses below 750 r (so-called stimulating dose) may excite the liberation of a stimulating hormone which affects the islet cells of the pancreas rather than causes a depressing effect on diabetogenic activities of the anterior lobe. Or we may theorize on the

basis of the general claims of Fränkel[11] that the supposedly hyperfunctioning hypophysis in diabetes mellitus is more sensitive to roentgen rays than is the normal hypophysis of the experimental dog.

In considering the effect of massive irradiation of the hypophyseal area, cognizance must be taken of the anatomical and functional relationship existing between the hypophysis and the hypothalamus immediately above. In the latter are

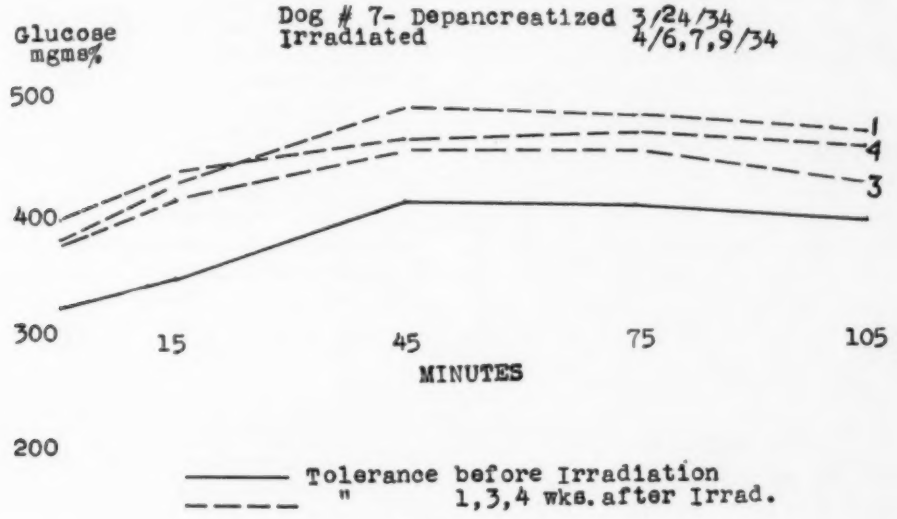

Chart III

centers controlling various important metabolic processes, such as water exchange, heat regulation, and particularly the mobilization of glycogen from the liver. Massive irradiation must necessarily act on these nervous centers as well as on the hypophysis itself. Consequently any change which follows massive irradiation of the brain in this vicinity may not be due to the effect on the hypophysis alone but to the vegetative centers on the hypothalamus as well.

Whatever the explanation of the failure of these experiments may be, they sound a note of warning to workers contemplating the treatment of diabetes mellitus by massive irradiation of the hypophysis. Massive doses of roentgen rays which one would not employ in treating patients seem to have very little or no inhibitory effect on the diabetogenic activity of the gland; a third of this dose to the skin, however, produces severe second degree burns. What immediate or delayed effects these heavy doses have on nerve structures and on other hormones elaborated by the hypophysis cannot be easily determined. Thus it seems to us that the radiation treatment of diabetes mellitus requires a better rationale, which can proceed only from a more exhaustive clinical and experimental study of the details of the hypophysis-pancreatic interrelationship, and that less than 750 r delivered to the gland is advisable.

It is our plan to irradiate the hypophyseal area with systematic graduated doses in an effort to determine if the irradiation has a stimulating control.

Further we are desirous of determining in depancreatized animals if graduated doses below 750 r exert a stimulating effect.

Further we hope to learn something by subtotal removal of the pancreas, waiting for a time when the remaining tissue begins to falter in its function, irradiate the hypophysis by small graduated doses in an effort to see if a stimulating hormone can be produced which will effect the metabolic process.

SUMMARY

In five of seven diabetic (depancreatized) dogs the fasting blood sugar was not reduced after irradiation of the hypophyses by high dosage. In three animals the blood sugar was considerably higher after irradiation.

The response to ingested glucose was always typical of severe diabetes.

There was no increased sensitivity to insulin, and the insulin dosage necessary to prevent glycosuria on a well-controlled diet could not be reduced.

No indication, then, was found that massive roentgen irradiation of the hypophysis, under the conditions stated, reduces the severity of the symptoms of experimental diabetes.

Massive irradiation (over 750 r) is contraindicated in patients with clinical diabetes.

We wish to express our indebtedness to Dr. John Pilcher of the Department of Pathology for the histological studies reported in the paper.

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DIFFRACTION STUDIES OF THE EFFECT OF SODIUM FLUORIDE AND PARATHORMONE UPON THE INCISORS AND TIBIAE OF RATS

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THIS study was undertaken to determine the nature of the change in rats' teeth when sodium fluoride was included in the diet. Later, the study was enlarged to include similar work with the tibiae of the rats. The interest in this work was centered on the structural changes such as crystal structure, orientation, and particle size, as affected by diets containing sodium fluoride,* injection of parathormone,† and combinations of the two, and also a mixture of sodium fluoride with aluminum sulphate.** In addition, observations were made on the teeth of both normal and rachitic rats.‡

Research carried out at the University of Arizona[1,2,3] has shown that the "mottling" of teeth is due to fluorides in drinking water. Localities in the United States where fluorides are found in the water in amounts sufficient to cause mottling have been carefully mapped out by Smith, Lantz and Smith.[2] Bowes and Murray[4] have done a similar piece of work for Maldon, Essex, England.

Rats were chosen as the experimental animals for this research since their incisors are readily affected by the fluoride and require only about four weeks[5] to renew themselves. McCollum, Simmonds, Becker and Bunting[6] were the first to use rats for a study of fluoridism. They have reported chemical changes in bone and teeth. Schour and Smith[7] have described in detail the histological changes in the incisors of rats when the fluoride was given by injection.

The outward changes in the teeth produced by fluorides are mottling of the enamel, loss of luster, and yellowish color with a change to a chalky white brittleness and retardation of growth.[8,9,10]

Roentgen-ray diffraction methods lend themselves best to the determination of structural changes with which we are especially concerned in this work. A large part of the evidence from previous investigation[11–22] indicates that enamel and dentin structures are identical with that of the mineral apatite (a natural calcium phosphate containing a little fluorine or chlorine). There is considerable dispute as to whether apatite is the principal constituent of teeth and bone or whether the composition is a mixture of apatites or of apatite and another compound. Henschen, Straumann and Bucher[11] suggest that there is a mixture of two inorganic substances, one of which has a structure similar to apatite. DeJong[12] and Taylor and Sheard[13] offer the general formula $3Ca_3(PO_4)_2 \cdot CaX_2$ where X represents Cl^-, F^-, OH^-, $\frac{1}{2}O^{--}$ or $\frac{1}{2}SO_4^{--}$. Logan[25] gives X as representing $\frac{1}{2}CO_3^{--}$. Hendricks, Hill, Jacob and Jef-

* Colony diet[27]

	per cent
Wheat meal (entire kernel)	33.9
Yellow corn meal (entire kernel)	33.0
Whole milk powder	21.0
Old process linseed oil meal	7.0
Alfalfa leaf flour (green color)	2.0
Liver (vacuum dried)	2.0
Calcium carbonate ($CaCO_3$)	0.5
Sodium chloride (NaCl)	0.5
Yeast (irradiated or non-irradiated)	0.1

When sodium fluoride was added it was dissolved in water, mixed and dried on the corn meal, this replacing an equivalent amount of the corn meal (0.1 or 0.3 per cent of the diet).

† Parathormone (P-20) lot No. 881500–2 of Eli Lilly Company was used in 10 and 20 units per day.

** George R. Sharpless[26] kindly cooperated in furnishing specimens which had been fed sodium fluoride and aluminum sulphate.

‡ Rickets-producing diet (modified from Steenbock's No. 2965)

	per cent
Yellow corn meal	72.5
Wheat gluten	20.0
Sodium chloride (NaCl)	1.0
Yeast	3.0
Calcium carbonate ($CaCO_3$)	3.5

ferson[14] suggest the formula $Ca_{10}CO_3(PO_4)_6 \cdot H_2O$, and Hendricks, Jefferson and Mosley[15] offer $Ca_9(H_2O)_2(PO_4)_6$. Roseberry, Hastings and Morse[16] give the formula $CaCO_3 \cdot nCa_3(PO_4)_2$ where n is not less than two nor more than three. Thewlis[18] suggests the same structure as St. Naray-Szabo,[28] i.e. the unit cell of the apatite structure consists of two molecules of $CaF \cdot Ca_4(PO_4)_3$ or $CaCl \cdot Ca_4(PO_4)_3$. Bredig[26] and Klement and Trömel[27] conclude that a hydroxyapatite is the main constituent of bone. Moeller and Trömel[39] suggest that the enamel and dentin are different materials, the difference being either their crystal form, or the chemical composition of the material, or perhaps both.

The orientation of the material making up the enamel and dentin has already been studied by means of roentgen-ray diffraction patterns. Most of the specimens used were normal teeth of humans, dogs and swine. There is general agreement[16–22] that the enamel is oriented. Roseberry[16] says that the enamel is randomly oriented, at least in the samples which he used and which were cut normal to the axis of growth. Dentin has been found to be unoriented.[16,18,23,24] Thewlis[18–22] has done considerable work on the orientation of enamel in human and canine teeth. He has shown that the 001 axis of apatite lies at an angle of either 10° or 20° to the normal in human teeth. He suggests that the variation in the degree of orientation is a matter of the environment in which the enamel is formed, rather than of the conditions surrounding the tooth.

Little emphasis has been placed on the crystal size of the material making up the tooth or the uniformity of material throughout the length of a tooth except to say that the rods which are easily seen under the microscope are made up of colloidal material or very fine inorganic crystals. Bale, Hodge and Warren[23] have suggested that enamel crystals are of the order of 2.7×10^{-5} and dentin crystals 2.4×10^{-6}. Moeller and Trömel[39] give 10^{-4} as the size of enamel particles and 10^{-5} to 10^{-6} cm. as the size of dentin particles.

Most of the chemical analyses[2,6,9] of fluoride teeth and bone have been done to show the effect on the Ca:P ratio and total ash. Sonntag,[30] Kick et al,[38] and Bowes and Murray[41] have shown that fluorine administered in forms other than calcium fluoride produces an increase in the percentage of fluorine in teeth and bones of animals.

The suggestion has been made that parathyroid or thyroid glands, or both, are directly affected by sodium fluoride and that the "mottling" of the teeth is caused by the altered functioning of these glands.[31,32,33] Hauck, Steenbock and Parsons[34] say that there is no evidence of histological changes when parathormone is given. Sutro[35] and Schour and Smith[7] also find that there is no evidence in support of the above suggestion.

Recently, Sharpless[36] demonstrated the value of aluminum salts in preventing fluorine toxicosis in rats. Sufficient sodium flouride (0.1 per cent of diet) to depress the growth and cause bleaching and pitting of the teeth when fed to animals was nontoxic when fed with a diet containing 2 per cent aluminum chloride. Since aluminum is not absorbed by the rat it is assumed that this protective action must take place in the intestinal tract, probably by the formation of a very slightly dissociated aluminum-flourine compound. Aluminum sulphate appears to be similar to aluminum chloride in preventing fluorine toxicosis.

EXPERIMENTAL

The animals used in this study were healthy young stock rats prepared in the Research Laboratory of the Children's Fund of Michigan.* The heads of the animals were kept in formalin for more than two months. Heads of rats given sodium fluoride and aluminum sulphate alone and in combination, were furnished by the laboratory of the Henry Ford Hospital. The latter specimens had been kept in formalin a shorter period.

* The rats were prepared by Helen A. Hunscher and Icie G. Macy.

The study of the tibiae was limited to those from normal rats, rats having rickets, and rats fed a diet which contained 0.3 per cent sodium fluoride, excess parathormone, or combinations of the two.

The carefully extracted whole teeth were mounted with collodion on small pieces of wood. For the reflection patterns the tooth was cleaned with acetone and then mounted with plastilina directly over the lower half of the pin hole. The enamel was scraped off, exposing the dentin for the dentin reflection pictures. Longitudinal sections were made by sandpapering the teeth between two pieces of wood. Special care was taken to wear the tooth evenly so that the middle section would be left. Sections about 0.1 mm. in thickness were mounted over the pin hole, using lubriseal. Cross sections of the same thickness were made by slowly grinding down a section of tooth mounted on a piece of wood with collodion. Decalcification was accomplished by treating the specimen with 0.1 per cent hydrochloric acid for short intervals. The acid was used four consecutive times for thirty seconds each, then once for one minute, once for seven minutes and the last time for twenty minutes, making a total of thirty minutes' treatment. A microscopic examination was made after each treatment with acid and before the roentgen-ray pattern was made.

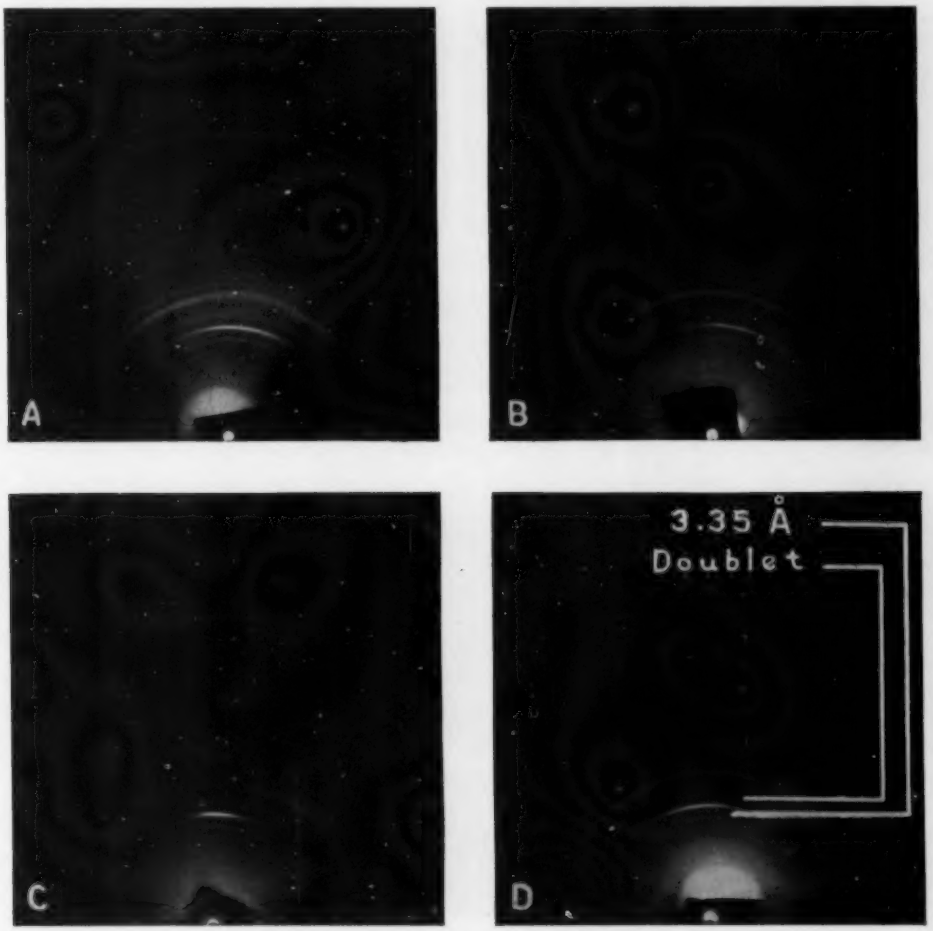

Fig. 1. A, tip of upper incisor of normal rat; B, upper incisor of rat fed diet containing 0.1 per cent NaF; C, tip of lower incisor of normal rat; D, lower incisor of rat fed diet containing 0.1 per cent NaF.

Reflection and transmission diagrams were made of a human tooth by preparing and mounting the samples in the same manner.

The preliminary work on the incisors was done with a molybdenum target General Elec-

tric tube. The greater part of the later work was done with a copper target, Philips tube. In both cases the pin hole in front of the collimator was about 0.5 mm. in diameter, and the one in back of the collimator, next the roentgen tube, was 1 mm. in diameter. Distances of 3 and 5 cm. between the specimen and the film were used. Exposure time with the copper target tube varied from one to three hours, depending upon the type of sample used. With the molybdenum target tube the exposure required was twenty-four to thirty-six hours. Flat films were used for all work. Both tubes were run at 20 ma. and 34 kv. A zirconium oxide filter was used on the molybdenum target tube and one of nickel oxide on the copper target tube.

Artificial chlorapatites and fluorapatites were made by fusing, in graphite crucibles, the required amounts of calcium phosphate $Ca_3(PO_4)_2$ with calcium fluoride or calcium chloride.

Qualitative tests for fluoride and carbonate were run on the natural apatites and normal and fluoride teeth. The fluoride tests were made by heating the samples with concentrated sulphuric acid and allowing the gas to come in

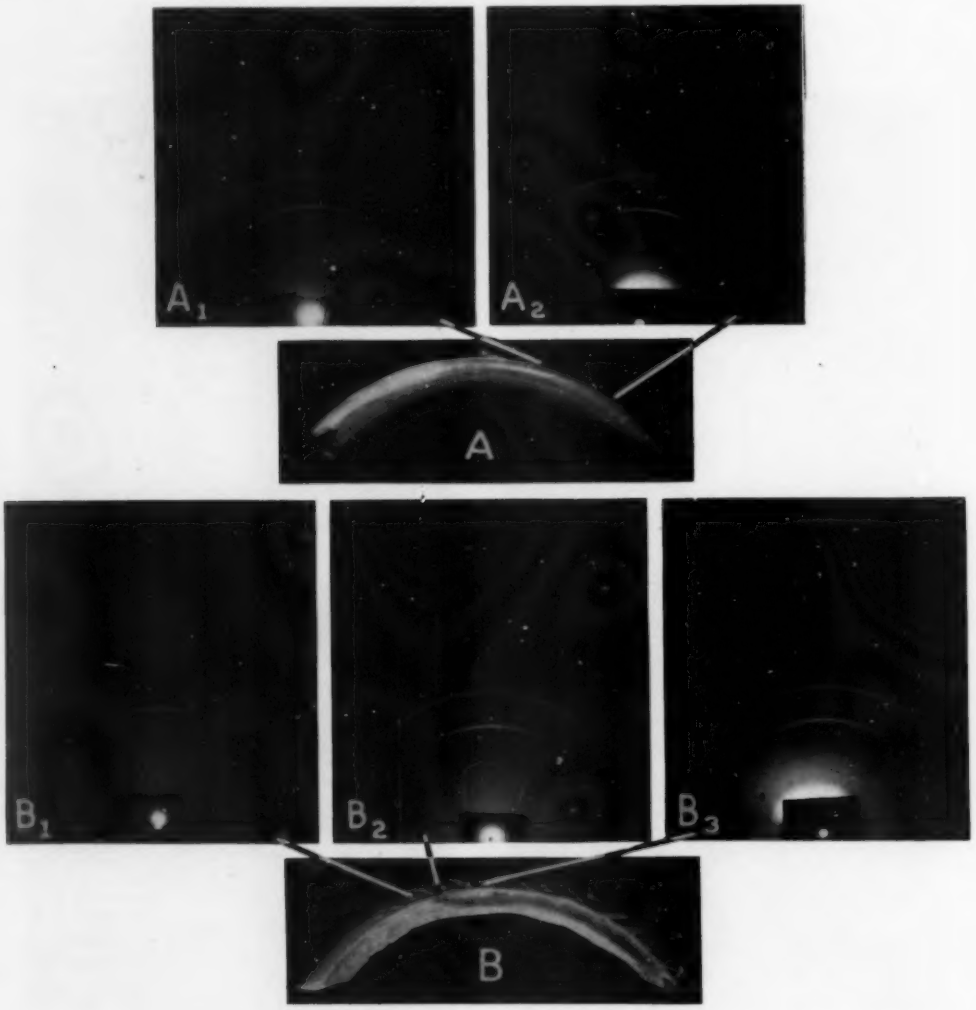

FIG. 2. A, normal lower incisor; A_1 and A_2, diffraction patterns from the approximate positions indicated in the diagram; B, lower incisor of rat fed on diet containing 0.1 per cent NaF; B_1, B_2 and B_3, diffraction patterns from the approximate position indicated in the diagram. Note that B_1 shows normal structure and B_2 and B_3 both show the presence of fluoride.

contact with a soft glass plate. The carbonate tests were made by allowing hydrochloric acid to react with the sample in a bottle which carried a hypodermic needle and syringe in the cork. The gas evolved was then measured in the graduated syringe. Both the cross sections and the surface of the teeth were examined in ultraviolet light and roentgenograms were made of several of the extracted teeth (Fig. 6).

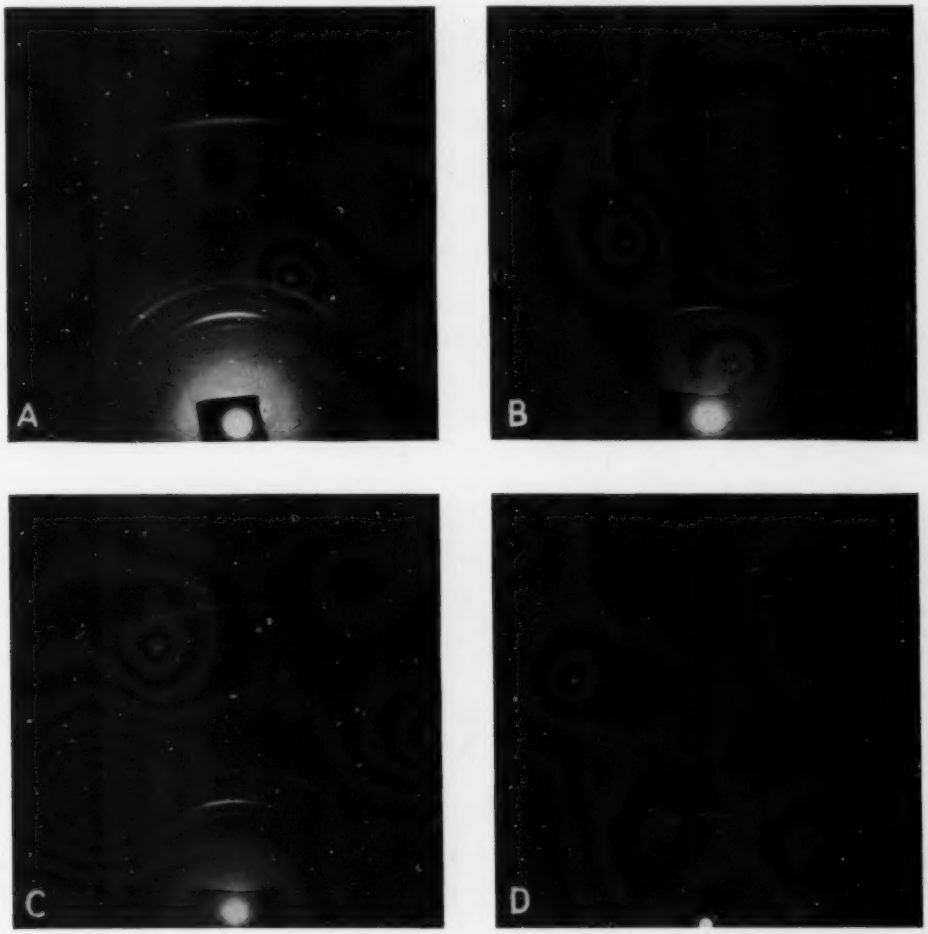

Fig. 3. Lower incisors of: A, rachitic rat; B, parathormone injected rat; C, rat fed on diet containing 0.3 per cent NaF, plus parathormone; D, rat fed on diet containing 0.1 per cent NaF both before and after the thyroid and parathyroid glands were removed.

Tibia cross section patterns were made with the molybdenum target tube from longitudinal sections. Since the patterns from these sections gave no data in addition to those obtained from other types of samples, little work was done with these cross section patterns. Powder samples were made from the epiphysis and the part of the bone immediately adjoining it, and from various samples taken along the shaft of the bone. Duplicate powder samples were made from the same parts of the bone mentioned above and the organic matter burned out by heating the bone to white heat. All powder samples were sifted through 200 mesh bolting cloth and then made up with collodion. Reflection patterns of the epiphysis of the tibia were made by holding the whole tibia in position with plastilina so that the convex part of the epiphysis was just in the roentgen beam. Roentgenograms showed the change in the density (Fig. 7) to be most pronounced in this part of the bone, and since the cross section patterns of the shaft showed no definite evidence of the fluorine, the epiphysis was the only part of the tibia used for reflection diagrams and for the unashed samples.

TABLE I

REFLECTION DIAGRAMS

(Radius in cm. CuK_α—3 cm.)

	Normal		Parathormone		Rachitic		0.1 per cent NaF		0.3 per cent NaF + Parathormone		0.1 per cent NaF – Thyroid
	Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Upper
1.							6.30				
2.					6.15	6.10		6.11			
3.		6.03									
4.							5.64				
5.		5.53			5.56				5.52*		
6.								5.46			
7.				4.70*		4.60*	4.70				
8.					4.60						
9.			4.20	4.24	4.16	4.18	4.21		4.20#		
10.	4.04	4.00	4.00	4.09	4.00	4.00	4.05	3.98	4.01	4.01	3.98
11.				3.88*							
12.						3.70*					
13.	3.50	3.46	3.50	3.55	3.48	3.50	3.54	3.50	3.54	3.50	3.48
14.	3.31	3.28	3.29	3.31	3.30	3.31	3.35	3.32	3.32	3.30	3.28
15.	3.20			3.20		3.20	3.21				
16.		3.13	3.18		3.14			3.18	3.17#	3.14	3.14
17.		3.00	3.00*	3.00	3.00	3.04	3.05	3.05	3.04#		3.02
18.	2.91		2.89	2.90		2.90	2.91		2.90#		
19.		2.85			2.86			2.83*		2.86	2.88
20.				2.70*			2.70*				
21.		2.66*					2.60*				
22.						2.50	2.50		2.49*		
23.		2.44		2.46	2.47			2.45#		2.43	2.40
24.	2.01	2.00	2.00	2.00	2.00	2.04	2.05	2.03	2.05	2.00	2.00
25.	1.90†		1.90†	1.86†	1.88†	1.90†	1.90	1.89	1.90		1.89
26.		1.85†								1.82	
27.	1.62†	1.60†	1.60†	1.61†	1.60†	1.62†	1.70 1.60	1.66 1.61	1.68* 1.60	1.70 1.60	1.66 1.58
28.	1.46	1.44	1.46	1.45	1.47	1.45	1.50	1.48	1.48	1.43	1.44
29.						1.40*	1.42*		1.40	1.34#	1.40#
30.	1.30	1.30	1.30	1.30	1.30	1.30	1.32	1.30	1.31	1.26	1.28

† Line rather broad. Underscored for greatest intensity. * Very light line. # Light line. { One line dividing.

RESULTS

The qualitative tests showed an appreciable amount of fluorine in the fluoride teeth, but not enough in the normal teeth to give a good test. This is, in general, in agreement with the quantitative analysis made by Kick et al,[38] who have shown that there is a trace of fluorine in normal pigs' teeth, with the amount increasing in direct proportion to the fluorine in the diet. The artificial and natural fluorapatites gave good tests but neither of the chlorapatites gave a positive reaction to a test for fluorine. Staffelite, a natural carbonate apatite, gave a definite fluoride reaction. Staffelite and the teeth were positive for carbonate, the staffelite giving the theoretical volume of carbon dioxide, the teeth showing small amounts. Neither the natural nor the artificial fluorapatites nor chlorapatites gave any carbon dioxide.

The natural fluorapatites and chlor-

TABLE II

REFLECTION DIAGRAMS

Spacing in Ångström Units. CuK_α—3 cm.

	Normal		Parathormone		Rachitic		0.1 per cent NaF		0.3 per cent NaF + Parathormone		0.1 per cent NaF – Thyroid
	Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Upper
1.		1.46			1.46	1.46		1.46			
2.		1.52		1.60*	1.50		1.44				
3.					1.61	1.61	1.49	1.51	1.51		
4.							1.60				
5.			1.67	1.68	1.68	1.68	1.68		1.68		
6.	1.72	1.73	1.72	1.70	1.72	1.73	1.71	1.73	1.72	1.72	1.72
7.				1.76*							
8.	1.84	1.85	1.84	1.83	1.85	1.84	1.83	1.84	1.83	1.84	1.85
9.	1.90	1.91	1.91	1.91	1.91	1.91	1.89	1.90	1.90	1.91	1.91
10.	1.95	1.97	1.95	1.95	1.96*	1.95	1.94	1.96	1.96#	1.97	1.96
11.	2.04	2.01	2.01*	2.01	2.01	2.00	1.99	1.99	1.99#		2.00
12.		2.07	2.06	2.05	2.07	2.05	2.04	2.08*	2.05#	2.07	2.06
13.		2.17*		2.14*			2.14*				
14.							2.20*				
15.		2.30		2.29	2.28	2.26	2.26	2.30	2.27	2.31	2.33
16.	2.65	2.65	2.66	2.65	2.66	2.61	2.61	2.63	2.61	2.65	2.65
17.	2.76†	2.82†	2.76†	2.77†	2.78†	2.76†	2.76†	2.77†	2.76†	2.85†	2.77†
18.	3.19†	3.17†	3.18†	3.15†	3.18†	3.14†	3.02 3.14	3.08 3.16	3.04 3.14	3.02 3.18	3.08 3.21
19.	3.45	3.47	3.43	3.45	3.41	3.45	3.35	3.39	3.39	3.49	3.47
20.						3.50*	3.55		3.55	3.68	3.55
21.	3.78	3.78	3.78	3.78	3.78	3.78	3.74	3.78	3.76	3.89	3.81

† Line rather broad. Underscored for greatest intensity. * Very light line. # Light line. { One line dividing.

apatites were used as standards for the diffraction measurements. The spacings of the artificial apatites agreed with those of the natural.

Powdered, pure sodium chloride was used to standardize the apparatus. For spacings of greater length, about 3.1 Å, there is an error of ±0.04 Å, while the shorter spacings, about 1.61 Å gave an error of ±0.005 Å. All calculations of spacings were made by using Bragg's equation $n\lambda = 2d \sin\theta$ where n is the order of reflection, λ the wave length, and d the spacing. All calculations in Table III were made using 1.54 as λ, the wave length of copper, and with the film 3 cm. distant from the specimen.

From Tables III and IV it can be seen that the enamel of all the teeth used is in a definite apatite structure. By a comparison of the spacings, it can be concluded that the apatite is a halogen or carbonate apatite mixture. No conclusions can be drawn as to the possible hydroxyapatite structure. The last column in Table IV gives the spacings for calcium fluoride. A comparison of these spacings with those of the fluoride teeth shows that there is probably a deposit of calcium fluoride, as such, in addition to the apatite structure of the normal teeth. It will be noted in Figure 1D that the 3.36 Å line shows more than it does in Figure 1B. The 3.36 Å spacing seems to be intensified by an increased feeding of sodium fluoride. In fact, in some instances in the lower fluoride diets, there seems to

TABLE III

SPACINGS IN ÅNGSTRÖM UNITS

	Staffelite	Natural Fluor-apatite	Natural Chlor-apatite	Hendricks F-Cl apatite	St. Naray Fluor-apatite	Roseberry Fluor-apatite	Chlor-apatite	Dahlite	CaF_2
1.					1.42				
2.					1.44				
3.					1.46				
4.					1.50	1.49	1.49	1.49	
5.						1.53	1.52	1.51	
6.				1.61	1.60				1.60
7.				1.69	1.71	1.71	1.71		
8.	1.73				1.74	1.75	1.75		
9.						1.79			
10.	1.83	1.81	1.81	1.81	1.83	1.83	1.82	1.83	
11.	1.88			1.85	1.87	1.88	1.88	1.87	1.87
12.		1.93	1.90	1.91	1.93	1.93	1.93	1.93	
13.	1.94		1.96	1.96					
14.		2.02#	2.05#	2.04		2.05	2.02		
15.	2.14	2.11#	2.17#	2.17	2.12	2.13	2.13	2.12	
16.			2.30	2.31					
17.	2.25	2.23			2.24	2.25	2.26	2.24	
18.	2.63		2.61#	2.65	2.60	2.60	2.60	2.60	2.58
19.					2.72	2.72	2.72	2.72	
20.	2.79	2.76	2.79	2.78					
21.				2.86					
22.					3.02	3.02	3.05	3.02	3.02
23.	3.10	3.08	3.10	3.08					
24.						3.15	3.15		
25.			3.36		3.35		3.35	3.35	3.36
26.	3.47	3.40		3.42		3.40			
27.				3.54†					
28.		3.65							
29.	3.79				3.75			3.75	
30.						3.85	3.81		3.82
31.									3.89

† Calculated spacing.
# Light line.
Natural samples from Ward Natural Science Establishment, Inc., Rochester, N. Y.

TABLE IV

DECALCIFICATION OF LONGITUDINAL SECTION

Spacing in Ångström Units. CuK_α—5 cm.

Untreated	0.1 per cent NaF Lower incisor treated with 0.1 per cent HCl						
	0.5 min.	1 min.	1.5 min.	2 min.	3 min.	10 min.	30 min.
3.79	3.82	3.74	3.76				
3.36	3.40	3.40	3.35	3.40	3.40	3.40	3.36
3.08	3.05	3.05	3.05	3.10	3.04	3.10	
2.78	2.78	2.78	2.75	2.77	2.70	2.70	2.75
					2.58	2.54	

TABLE V

DECALCIFICATION OF LONGITUDINAL SECTION

Spacing in Ångström Units. CuK_α—5 cm.

Untreated	Normal lower incisor treated with 0.1 per cent HCl						
	0.5 min.	1 min.	1.5 min.	2 min.	3 min.	10 min.	30 min.
3.72	3.72	3.74					
3.40	3.40	3.40	3.35	3.36	3.35	3.35	
3.10	3.08	3.05		3.14			
2.78	2.78	2.78	2.76	2.78	2.76	2.70	

be no calcium fluoride at the spot where the roentgen ray hit the tooth. This 3.36 Å spacing might be accounted for on the basis of a chlorapatite structure, but since it does not appear in the normal diagrams the conclusion may be drawn that the normal tooth enamel is a fluorapatite mixture and that the 3.36 Å spacing is due to calcium fluoride. This conclusion is supported by the fact that other calcium fluoride spacings appear in the pattern, but are coincident with the apatite spacings

TABLE VI

REFLECTION DIAGRAMS

Taken Lengthwise of Tooth

Spacing in Ångström Units. CuK_α—3 cm.

	Normal upper incisor				0.1 per cent NaF lower incisor			
	Tip	Tip	7 mm. from tip	Middle	Very tip	About 7 mm. from tip	Middle	Near middle
1.							1.45	
2.							1.49	
3.							1.60	
4.				1.68			1.66	
5.				1.77				
6.	1.72	1.72	1.69		1.73	1.73	1.70	1.70
7.			1.80					1.82
8.	1.87	1.86	1.87	1.87	1.86	1.86		
9.	1.91	1.91	1.91	1.91	1.90	1.89	1.88	1.89
10.						1.95	1.95	1.94
11.						1.98	1.96	1.98
12.					2.06		2.01	2.03
13.		2.25	2.24	2.23				2.20
14.	2.32						2.28	2.32
15.			2.56	2.55				2.62
16.	2.66	2.64			2.66	2.61	2.61	
17.	2.82†	2.74†	2.75	2.74†	2.75†	2.75†	2.76†	2.75†
18.	3.14†		3.14†		3.18†	{3.05 3.12	{2.99 3.12	{3.04 3.13
19.		3.36			3.32	3.32	3.35	3.35
20.	3.39		3.40	3.39				
21.	3.78	3.78	3.78	3.78	3.78	3.75	3.78	3.76

† Line rather broad.
Underscored for greatest intensity.

{ One line dividing.

and not easily recognized. In many of the patterns of teeth from rats fed a diet including 0.3 per cent sodium fluoride and in some fed a diet containing 0.1 per cent sodium fluoride there is a shift in the first order reflection, shown by the separation of the wide line at spacing 1.62 ± Å in the normal, into two distinct lines 1.70 Å and 1.61 Å (Fig. 1D and Figs. 2B_2 and B_3). Roentgen diagrams taken lengthwise of the tooth showed some variation, especially in the fluoride teeth (Table VII).

TABLE VII

REFLECTION DIAGRAMS

Variable Composition

Spacing in Ångström Units. CuK_α—3 cm.

	0.7 per cent $Al_2(SO_4)_3 \cdot 18H_2O$				0.7 per cent $Al_2(SO_4)_3 \cdot 18H_2O$ + 0.01 per cent NaF			
	Upper incisor	Upper incisor	Upper incisor	Lower incisor	Upper incisor	Upper incisor	Upper incisor	Lower incisor
1.					1.63			
2.					1.64			
3.	1.72	1.72	1.71	1.70	1.72	1.70	1.71	1.71
4.	1.84	1.84	1.83	1.82	1.84	1.83	1.83	1.83
5.	1.90	1.90	1.89	1.88	1.89	1.89	1.89	1.89
6.	1.95	1.96	1.95	1.94		1.95	1.95	1.95 1.99
7.				1.98		1.97#		
8.				2.05				
9.		2.05	2.06			2.03	2.06	2.04
10.		2.26	2.26	2.24		2.26	2.26	2.26
11.	2.37				2.48†			
12.		2.62	2.62	2.61	2.66	2.62	2.62	2.62
13.	2.95	2.76 2.82	2.76	2.72 2.74	2.76	2.76	2.76	2.76
14.		3.13	3.13	3.18		3.17	3.13	3.18
15.	3.45	3.41 3.45	3.37 3.45	3.35 3.55#	3.35 3.49	3.39	3.37 3.45	3.41 3.55
16.	3.93	3.78	3.78	3.68	3.78	3.71	3.78	3.78

† Line rather broad. Underscored for greatest intensity. # Light line. { One line dividing.

The diagrams from the teeth of the rats fed aluminum sulphate and those fed combinations of aluminum sulphate and sodium fluoride all show the predominance of apatite structure. When 2.8 per cent of the diet was aluminum sulphate or when this percentage of aluminum sulphate was included in the diet with 0.01 per cent sodium fluoride, the 3.36 Å spacing, characteristic of chlorapatites and carbonate apatites, appeared. Since there are two lines, one 3.36 Å and the other 3.40 Å, this change would indicate that the aluminum may be keeping the fluorine in solution as an aluminum fluoride, or as some less dissociated aluminum-fluorine compound. This seems to be supported by the fact that the 3.40 Å line is still present when 0.7 per cent aluminum sulphate is fed, but in some instances the 3.36 Å also shows *very* faintly (see Table VIII). When 0.01 per cent sodium fluoride was fed with the 0.7 per cent aluminum sulphate, both lines usually appeared, as in the case of sodium fluoride previously noted. This could be accounted for by the fact that there is, apparently, not enough aluminum to take care of the fluorine in the normal enamel.

Less irregularity in composition is shown when aluminum sulphate is included in the diet than is shown in either the normal or sodium fluoride teeth (see Tables VIII and IX and Figs. 2, 4 and 6). However, there seems to be a decided tendency toward a more uniform composition when the larger amount of aluminum sulphate is included in the diet. Diffraction patterns were made of longitudinal sections of both normal and fluoride teeth. The sections were moved so that patterns were made at various places across the tooth as well as lengthwise of it (Fig. 4). The spacings of both agree with the reflection pictures, so that it may be concluded that both dentin and enamel are apatites, the normal probably a mixture as suggested previously, and the fluoride a mixture plus the calcium fluoride. The 3.40 Å spacing is again characteristic of the normal, while the 3.36 Å occurs in the fluoride. The normal is more consistently uniform than the fluoride, as suggested by the reflection diagrams also. This irregularity in the fluoride specimens is shown even more decidedly in the gradual decalcification of the cross sections. Tables V and VI give the spacings for the decalcified portions. Note that the normal consistently showed 3.40 Å through the one minute treatment and then consistently showed 3.36 Å. This indicates that the fluorapatite dissolves first, leaving chlorapatite or hydroxyapatite. It is further indicative of the fact that in fluoride teeth an unevenly stratified structure of different mineral substances is present.

TABLE VIII

REFLECTION DIAGRAMS

Variable Composition

Spacing in Ångström Units. CuK_α—3 cm.

	2.8 per cent $Al_2(SO_4)_3 \cdot 18H_2O$			2.8 per cent $Al_2(SO_4)_3 \cdot 18H_2O$ +0.01 per cent NaF		
	Upper incisor	Upper incisor	Lower incisor	Upper incisor	Upper incisor	Lower incisor
1.	1.70	1.71	1.72	1.71	1.71	1.71
2.	1.83	1.83	1.84	1.84	1.81	1.82
3.	1.89	1.89	1.89	1.90		1.89
4.	1.95	1.95		1.95		
5.		2.03	2.04			
6.	2.26	2.26			2.26	
7.	2.57					
8.		2.61	2.62	2.63		2.64
9.	2.75	2.76	2.75	2.76	2.70	2.76
10.	3.09	3.09				
11.			3.12			
12.	3.37	3.35		3.37	3.37	3.35
13.			3.41			
14.					3.66	
15.	3.78	3.78	3.78	3.78		
16.						3.84

Underscored for greatest intensity.

The crystal size of the normal and pathological enamel is slightly different as shown by films (Figs. 2 and 3). The spacing corresponding, approximately, to 3.14 Å gives a comparatively wide arc in both the parathormone and normal teeth. This is separated into two fine arcs in the patterns from the fluoride teeth, fluoride plus parathormone teeth, and the fluoride teeth from animals with the parathyroid glands out. Particles in the colloidal size range of 10^{-6} cm. or less give a broad, diffuse ring, while those particles between 10^{-3} and 10^{-6}

cm. give a sharp line.[40] Hence there seems to be a deposition of crystals larger than the colloidal size when sodium fluoride is included in the diet, but of colloidal size when normal diets or diets combined with injections of parathormone are given.

The orientation of both normal and pathological teeth is noticeably greater in the lower than in the upper incisors. This is true even in the teeth from rachitic rats. The degree of orientation of the latter would, of course, depend upon the degree of rickets. Upper incisors are almost entirely lacking in orientation in all cases (Fig. 1). There is a decided difference in the amount of preferred orientation. The fluoride lower incisors and the fluoride incisors from the rats from which the thyroid and parathyroids had been removed show practically no preferred orientation, while the 0.3 per cent sodium fluoride plus parathormone, the normal and the parathormone teeth are definitely oriented. Comparison of the three latter types (Figs. 1 and 3) classifies the parathormone as having the greatest degree of orientation, then the normal, and the 0.3 per cent sodium fluoride plus parathormone as having the least. The rachitic teeth may be classified anywhere in the scale depending upon the severity of the disease. The teeth we examined showed more orientation than the fluoride teeth, but somewhat less than the normal or 0.3 per cent sodium fluoride plus parathormone groups.

The longitudinal sections of the dentin of the lower incisors of both normal and fluoride teeth show that there is orienta-

TABLE IX

CHEMICAL EFFECT OF DIETARY TREATMENT UPON THE BONES OF RATS

Treatment of Rats	Average Chemical Composition of Fat-Free Tibia (Per cent)			Days on Treatment
	Calcium*	Phosphorus†	Fluorine‡	
Normal Colony diet Rapid gain in weight	23.3	11.4	0.02	83
Parathormone 10 units of parathormone were given for 3 days and 5 units per day thereafter	23.4	11.2	0.035	31
Rachitic Modified Steenbock diet No. 2965 Gained slowly in weight	19.2	7.7	0.11	41
Sodium fluoride (0.1 per cent) Started on 0.3 per cent NaF and after 10th day put on 0.1 per cent NaF Gained slowly in weight	21.5	10.2	0.91	87
Sodium fluoride (0.3 per cent) Very toxic effect of sodium fluoride evidenced by rapid loss of weight	18.8	8.8	0.42	10
Sodium fluoride and parathormone 0.3 per cent NaF for 10 days with final 3 days on 10 units parathormone. Lost weight	18.2	8.7	0.49	13

* *Calcium* was determined within an accuracy of 2 per cent of the value shown, i.e., in the first instance 23.3 ± 0.46. (Methods for the direct quantitative determination of sodium, potassium, calcium and magnesium in urine and stools. Tisdall, F. F., and Kramer, B. *J. Biol. Chem.*, 1921, *48*, 1.)

† *Phosphorus* was determined within an accuracy of 3 per cent of the value shown, i.e., in the first instance 11.4 ± 0.34. (Phosphorus metabolism; a system of blood phosphorus analysis. Youngburg, G. E., and Youngburg, M. V. *J. Lab. & Clin. Med.*, 1930, *16*, 158.)

‡ *Fluorine* was determined within an accuracy of 1 per cent of the value shown, i.e., in the first instance 0.02 ± 0.0002. (Volumetric method for determination of fluorine. Millard, H. H., and Minter, O. B. *Indust. & Engin. Chem.*, Anal. Ed., 1933, *5*, 7.)

tion, beyond a doubt (Fig. 4). There is no decided difference between the degree of orientation in normal and fluoride teeth. There is a tendency toward sharpening of the lines upon treatment with hydrochloric acid, however. This indicates that the smaller crystals are dissolving first, as would be expected. This same sharpening of the lines is not shown upon slow decalcification of the enamel. Cross sections of the tooth show no orientation (see Figure 5). This leads to the conclusion that there is a "fiber" structure, even in the dentin, which is oriented longitudinally at a small angle with the tooth axis.

Dentin of human teeth shows no orientation, either in the reflection longitudinal section or cross section patterns. This is in agreement with the results of other workers on this problem. It might be noted here that the relative amount of organic matter in the enamel of rats' and human teeth is very noticeable in the reflection pictures. Less organic matter is shown in the human than in the rats' teeth. Thewlis,[18–22] and Bale, Hodge and Warren[23] have made separate studies of the relative amounts of organic and inorganic matter in human

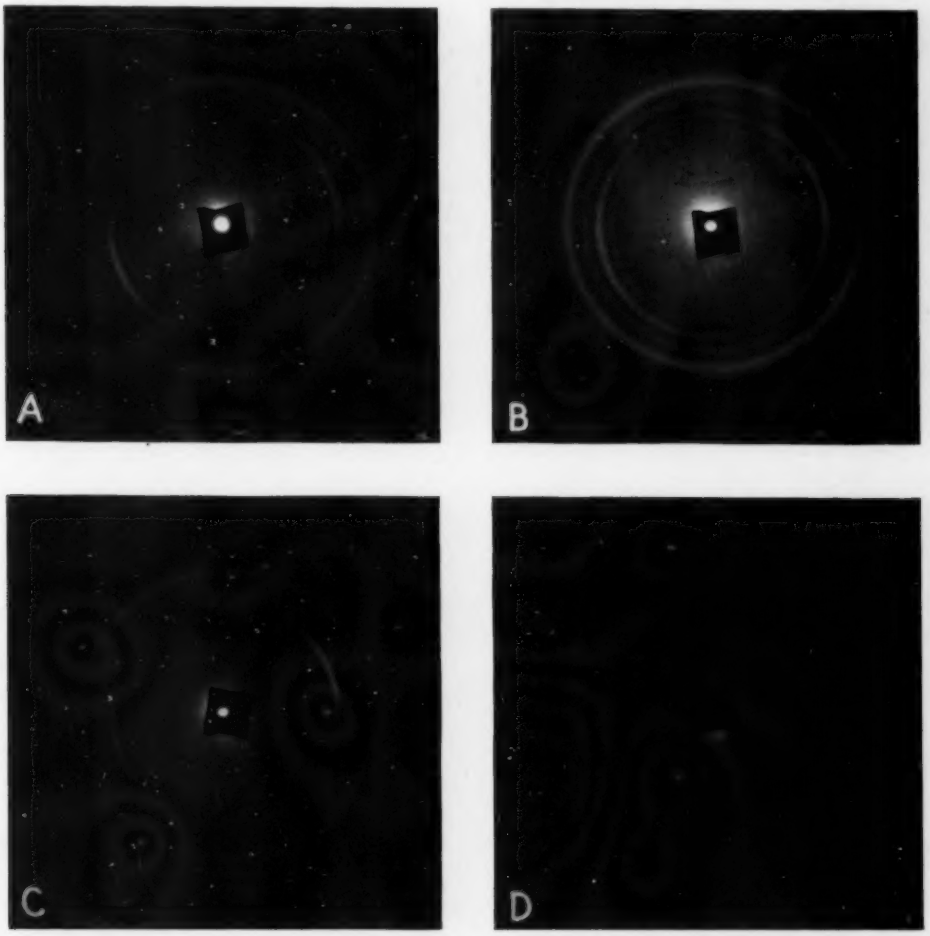

Fig. 4. Longitudinal section of a lower incisor of a rat fed on a diet containing 0.1 per cent NaF: A, middle of section, about 7 mm. from the tip; B, middle of section, and about 9 mm. from the tip; C, section cut 9 mm. from the tip and on the labial side of the middle; D, section cut 9 mm. from the tip and on the lingual side of the middle. Note: All of the above are dentin diagrams.

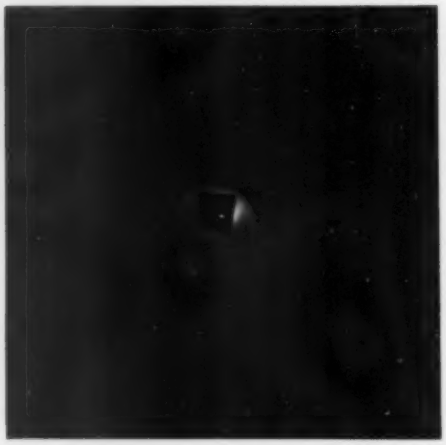

FIG. 5. Cross section of a lower incisor of a parathormone injected rat. The very slight amount of arcing is due to a small variation in the thickness of the sample.

teeth. The work for rats' teeth remains to be done. The roentgenograms (Fig. 6) indicate that there is an increase in density, and therefore inorganic matter, in the fluoride teeth. This is especially noticeable in the teeth of the rats that have been fed fluoride after having had the thyroid and parathyroid glands removed.* The deposition of free calcium fluoride in the haversian canals of the bone was demonstrated microscopically as early as 1891 by Brandl and Tappeiner.[42] Stanton and Kahn[43] in 1915 found crystals of CaF_2 in bone. No

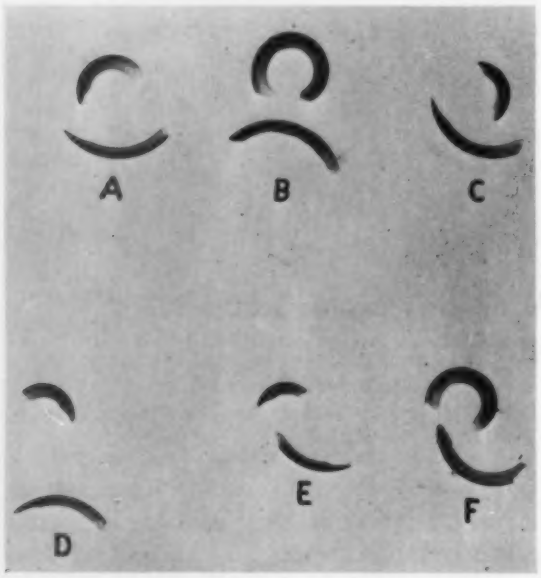

FIG. 6. Upper and lower incisors of: A, normal rat; B, rat fed diet containing 0.1 per cent NaF; C, rachitic rat; D, parathormone injected; E, rat fed diet containing 0.3 per cent NaF, plus parathormone; F, rat fed 0.1 per cent NaF and having thyroid and parathyroid glands removed.

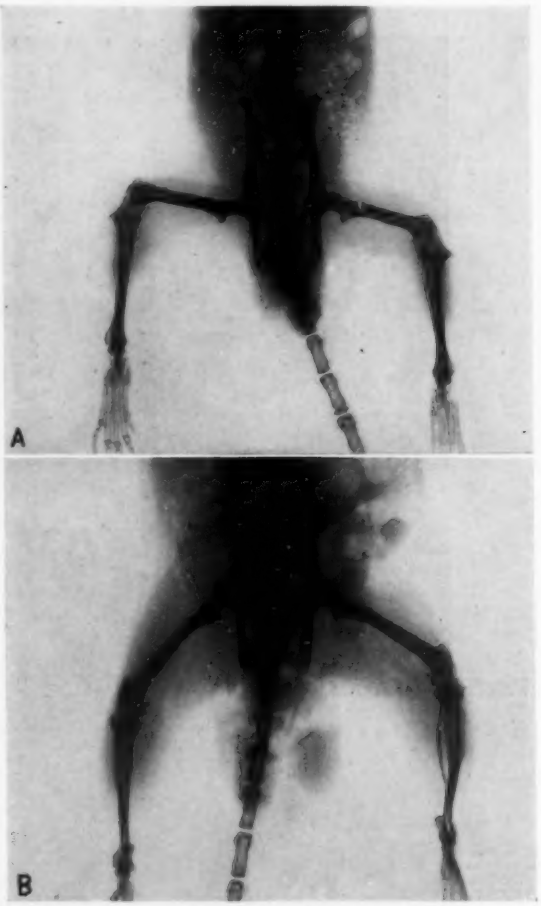

FIG. 7. Roentgenogram showing tibiae. A, rat fed 0.3 per cent sodium fluoride; B, rat fed 0.1 per cent sodium fluoride.

mention was made of stratification in either report.

Reflection diagrams of the epiphysis indicate that there is practically no preferred orientation at that point of the bone, for the arcs are continuous and uniform (Fig. 2). By looking closely at the various figures on this plate it can be seen that the arcs of the normal pattern (A), the parathormone

* The parathyroid-thyroidectomies were performed by C. N. Weller, M.D. of the Department of Surgery of the Children's Hospital of Michigan.

(c), and the parathormone plus the 0.3 per cent sodium fluoride diagram (B), seem slightly wider than those of the tibiae of the rats fed on the diet containing 0.3 per cent sodium fluoride (D). This would indicate that there is a tendency in the bone This is in contrast to the patterns of the enamel of the teeth, for even the normal teeth showed irregular composition of enamel deposits.

The results given in Table x are measurements calculated from Bragg's equation

TABLE X

COMPARISON OF DATA OBTAINED FROM REFLECTION, AND POWDERED UNASHED AND ASH PATTERNS OF TIBIA

Spacing in Ångström Units. CuK_a—3 cm.

	Normal			Parathormone			Rachitic			Parathormone +0.3 per cent NaF			0.3 per cent NaF		
	Reflection	Powdered		Reflection	Powdered		Reflection	Powdered		Reflection	Powdered		Reflection	Powdered	
		Unashed	Ashed		Unashed	Ashed		Unashed	Ashed		Unashed	Ashed		Unashed	Ashed
1.															8.08
2.			7.80			7.87						7.91			
3.									7.5						
4.						6.40			6.90						
5.			5.13			5.18			5.18						
6.	3.78#			3.81			3.76			3.71*			3.79		3.72
7.	3.45	3.45	3.43	3.45	3.41	3.45	3.39	3.46	3.41	3.38	3.45	3.45	3.50	3.41	3.49
8.						3.18‡									3.12‡
9.	3.11	3.07	3.05‡	3.09	3.10		3.02	3.13	3.15	3.11	3.09	3.06		3.09	
10.	2.77	2.76	2.78	2.78	2.81	2.81	2.75	2.81	2.79	2.76	2.81	2.78	2.79	2.79	2.82
11.			2.60#			2.59‡	2.57		2.58				2.67#		2.70§
12.															2.52§
13.	2.30#	2.26	2.24	2.30#	2.28	2.27		2.28	2.24	2.26†	2.26	2.26	2.26*	2.28	2.28
14.			2.13			2.14			2.13			2.13			2.16
15.	1.96		1.93	1.97	1.96	1.94#			1.94	1.91		1.93	1.95#		1.96
16.	1.84*		1.87	1.84#		1.87	1.80			1.84*		1.87	1.84		1.84
17.			1.82		1.82										
18.	1.83		1.71	1.73		1.71	1.70		1.71	1.72		1.70	1.72		1.72

† Line rather broad. * Very light line. # Light line. ‡ Characteristic spacings. § Fine.

as in the teeth for the sodium fluoride to form slightly larger crystals. The rachitic pattern shown here seems to agree with that of the fluoride. However, this was found to be the case only when 0.1 per cent sodium fluoride was included in the rachitic diet.

The only composition irregularity in patterns of similar types of bone was noted in the shaft of the parathormone injected rats. The normal tibiae seemed to be almost, if not entirely, uniform. The only patterns which showed any irregularity were those of the ashed samples. and each figure is an average value for three to six films.

DISCUSSION

It is clear, then, that the fluoride teeth have a heterogeneous composition of the apatite-like material of normal teeth and calcium fluoride These mineral salts are not deposited in a uniform mixture but rather, even in the case where animals have been fed a uniform diet containing a small quantity of soluble fluoride for a long period of time, the teeth are stratified and contain uneven patches of fluoride

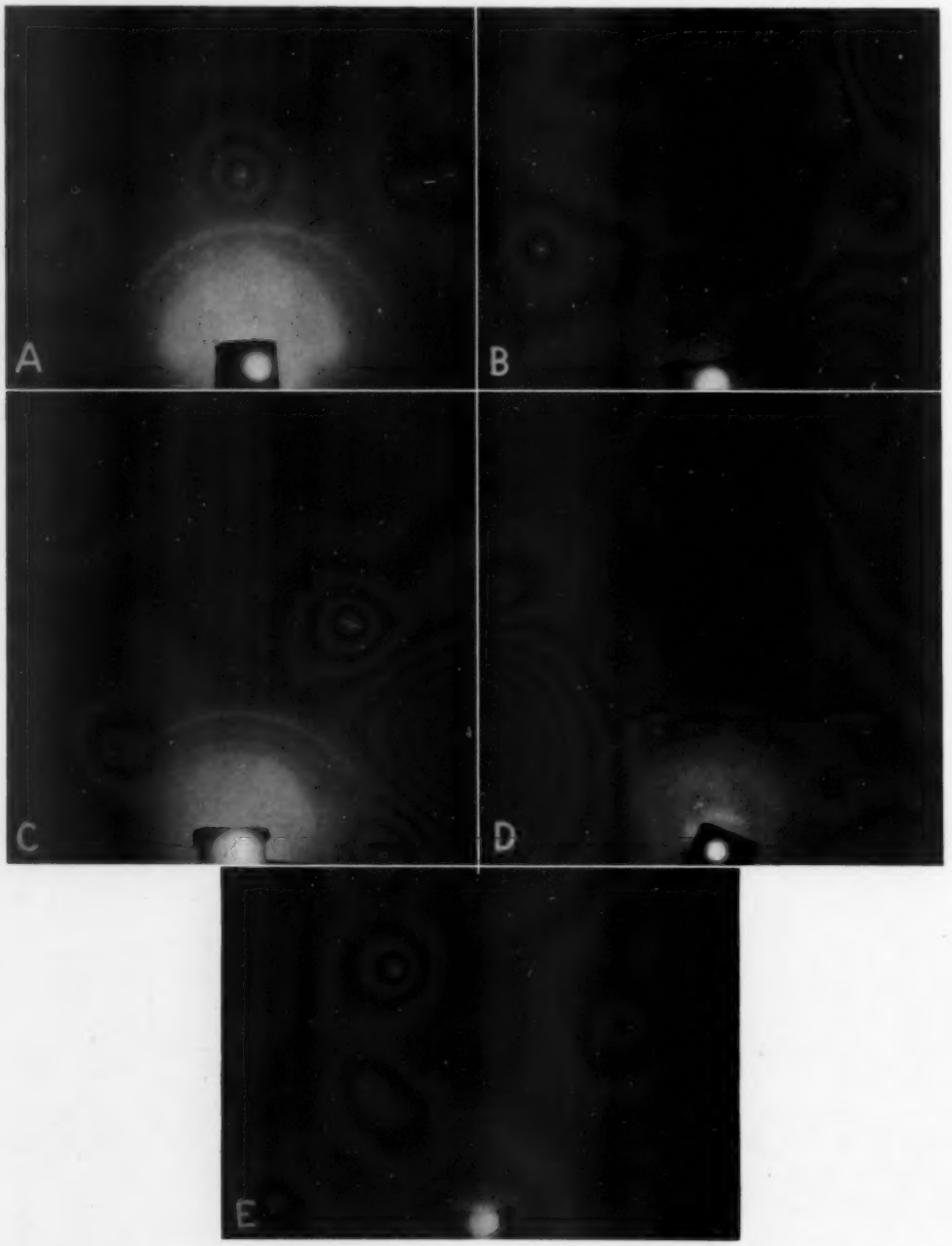

FIG. 8. Reflection patterns of epiphysis. A, normal rat; B, rat fed 0.3 per cent sodium fluoride plus parathormone; C, rat injected with parathormone; D, rat fed 0.3 per cent sodium fluoride; E, rachitic rat.

material. It is an additional characteristic of these teeth that they lack a fiber structure and are not uniformly oriented along a fiber axis, as are normal teeth. This is sufficient explanation for the fact that these fluoride teeth lack mechanical strength and are easily broken. This condition is demonstrated conclusively by the variation in the roentgen-ray diffraction pattern along the length of the tooth, either on the surface or in longitudinal section but especially in those sections

treated with hydrochloric acid. These findings are further borne out (1) by the uneven and spotty erosion of these teeth both in the animal's mouth and in dilute HCl in the laboratory, and (2) by the appearance of dark bands and patches in the normal blue-green fluorescence of the teeth under ultraviolet light, even though no banding but only the characteristic chalky appearance of fluoride teeth can be seen in visible light.

The fact that fluoride teeth appear greatly elongated in comparison to the normal ones is not due to an excess rate of growth but to decreased rate of wear. These teeth, while brittle, contain layers of a material which is abnormally hard.

It is also demonstrated that the injection of excess parathormone causes the mineral material of the teeth to be deposited in smaller crystals, with better orientation, than administration of sodium fluoride in the diet. In this way, parathormone tends to offset some of the ill effects of excess fluoride and produce teeth which are noticeably stronger and more uniform. The removal of the thyroid and parathyroids causes the fluoride to have a greater effect. However, the evidence obtained in this research does not settle the question of possible primary effect of fluoride on the thyroid-parathyroid glands, which then exert a secondary effect on

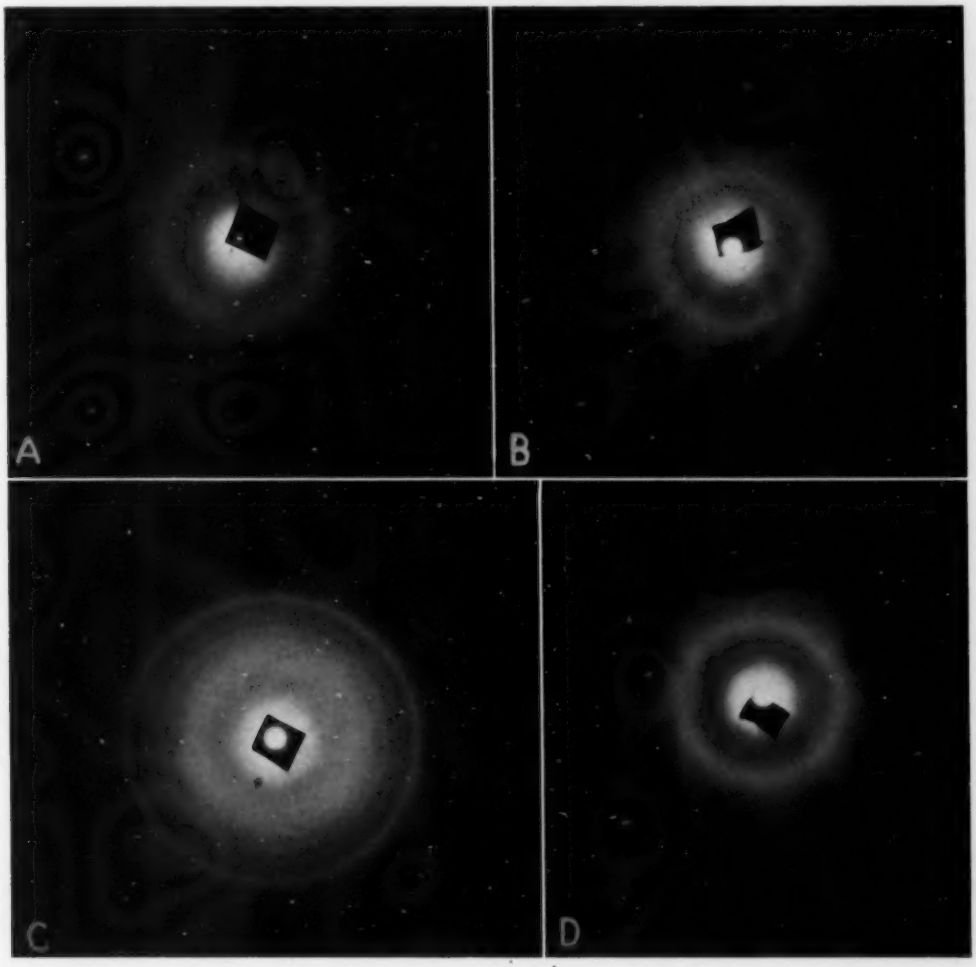

Fig. 9. Powder patterns, unashed epiphysis. A, normal rat; B, rat fed 0.3 per cent sodium fluoride plus parathormone; C, rat injected with parathormone; D, rat fed 0.3 per cent sodium fluoride.

tooth and bone structure.

The slight difference noted between incisors of the normal rats and those fed a diet containing 0.3 per cent sodium fluoride, i.e., the 3.36 Å line which appeared in the fluoride-fed rats' teeth and which was a slight shift from the 3.40 Å line found in the normal or parathormone teeth, did not show in any of the fluoride patterns for bone. This fact agrees with other evidence (rate of growth and change in orientation) to support the theory that teeth are affected more quickly than the bones of the body of the rat when fluoride is contained in the diet.

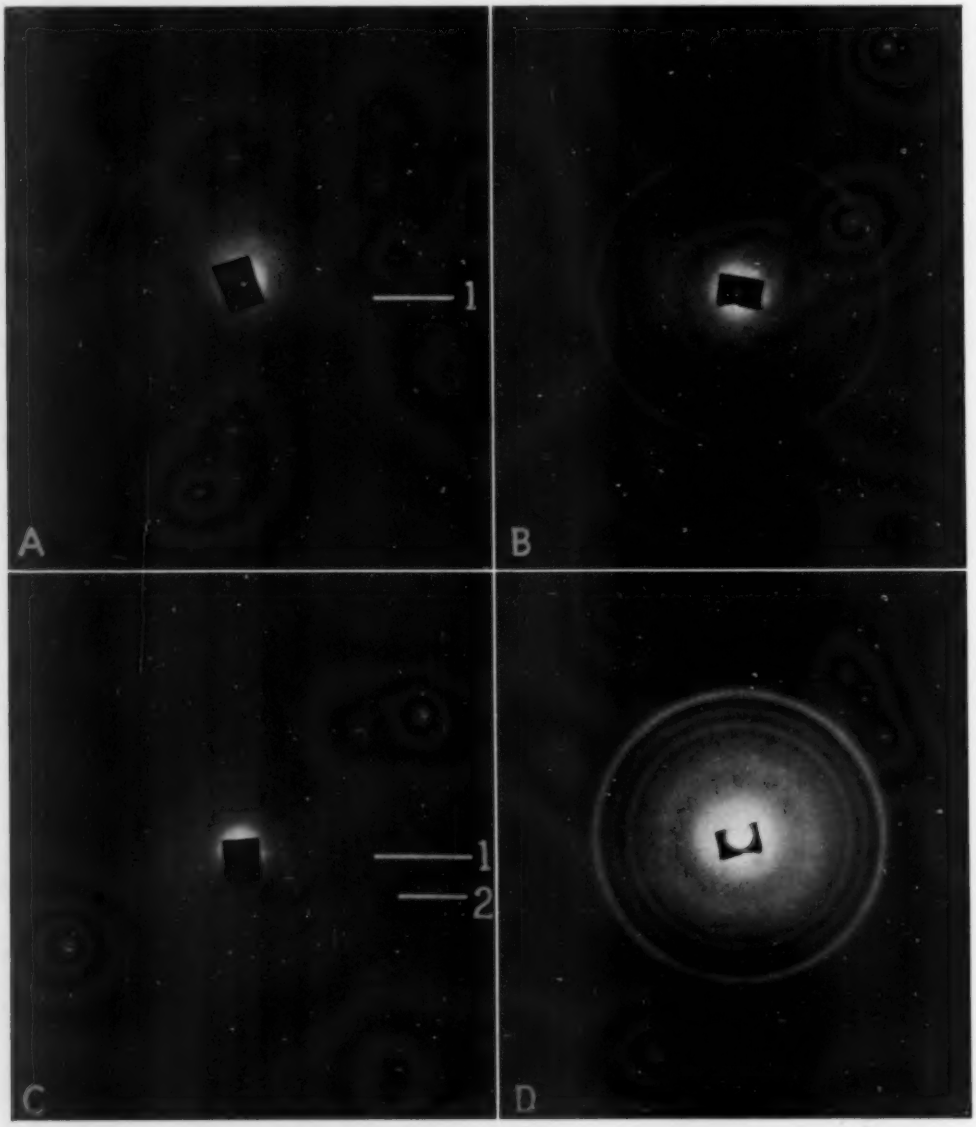

FIG. 10. Powder patterns, epiphysis ashed. A, normal rat; B, rat fed 0.3 per cent sodium fluoride plus parathormone; C, rat injected with parathormone; D, rat fed 0.3 per cent sodium fluoride.

All patterns, reflection, unashed powder, and ashed powder showed an apatite structure, as would be expected. There are no dependable differences between the normal and the pathological bone patterns as can be seen from the spacing values in Table X. This same uniformity may be noted in the

patterns in Figures 8 and 9. Figure 8 shows the reflection diagrams and Figure 9 the unashed powder patterns. Figure 8A is from a normal epiphysis, B is from an animal on 0.3 per cent sodium fluoride diet plus parathormone, C is parathormone, D is 0.3 per cent sodium fluoride and E is from a rachitic animal.

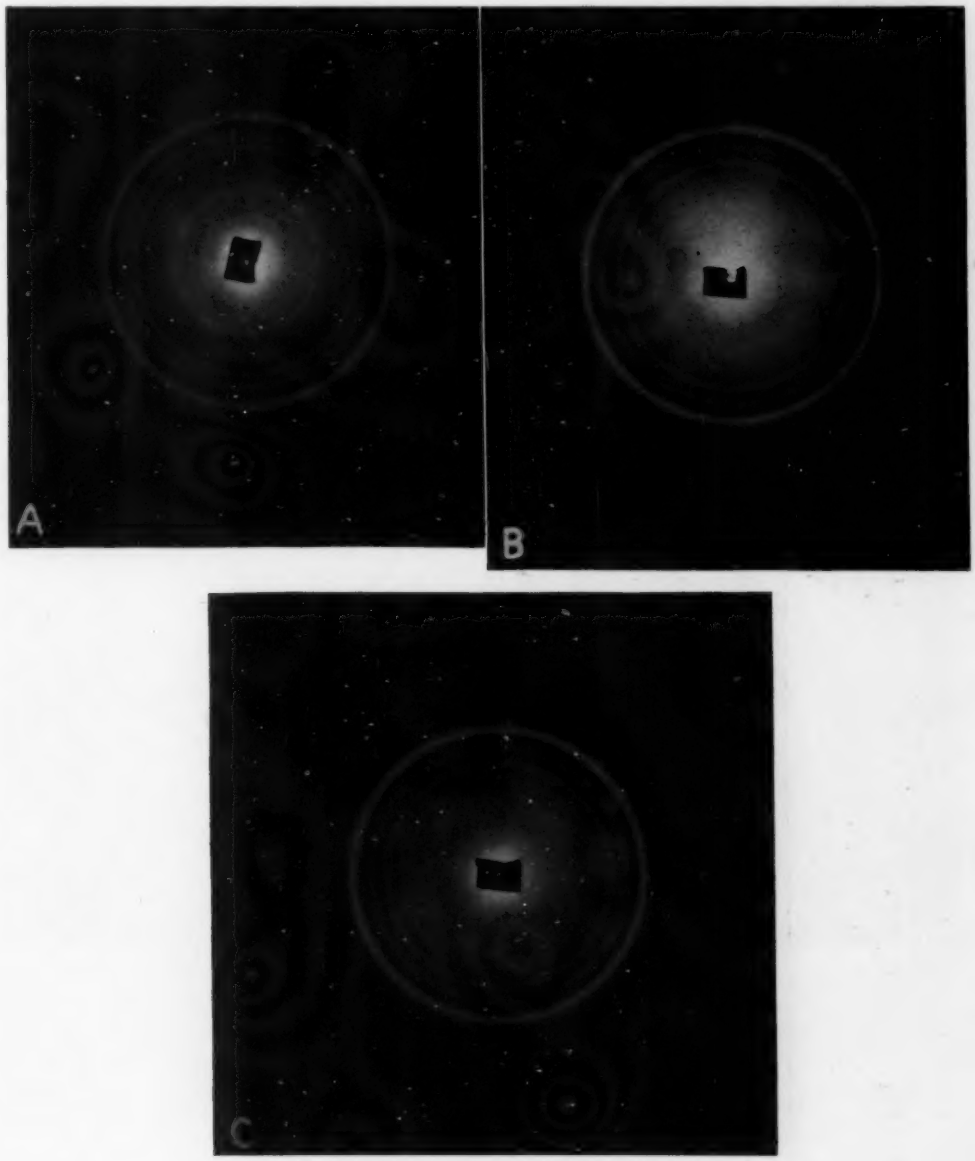

FIG. 11. Powder patterns, ashed epiphysis, rachitic rats.

The pattern of the powdered material is not clear or definite due to the fogging of the background by the organic matter. A comparison of Figures 9 and 10 shows the advantage gained by ashing the samples. Heating seemed to have no effect on the structure material of the normal epiphysis since the lines which can be measured on the unashed and those of the ashed samples are the same (see Table x, Figs. 8A and 9A). We may conclude, therefore, that if there is a change in pattern it is probably due to a pathological condition which shows in the ashed diagram, either be-

cause of the greater clarity or because the pathological bone is more easily affected by heat. In either case, the change of pattern indicates a change in bone structure.

shows this change in the parathormone pattern. This same shift was barely indicated by some of the data on the lower incisors. The asterisk(*) is placed near the

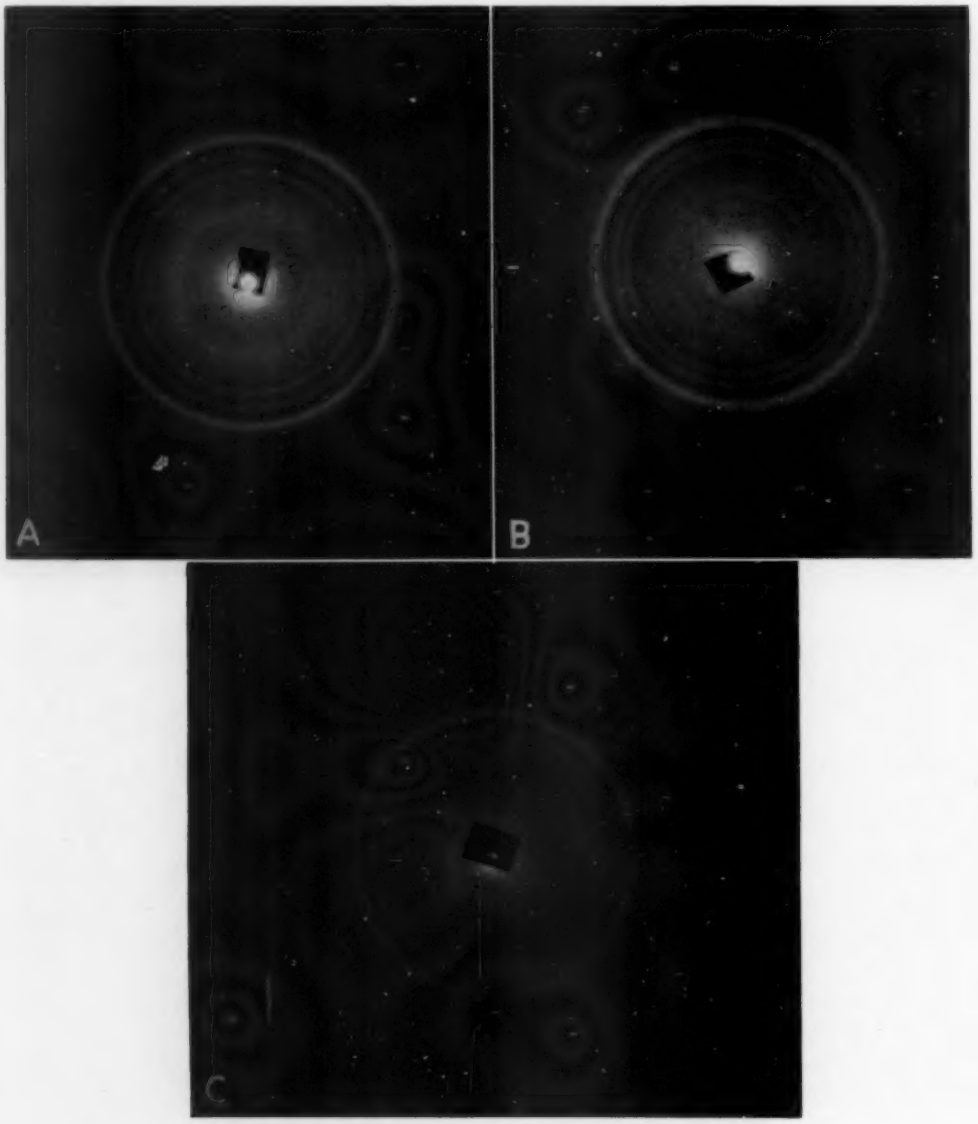

FIG. 12. Powder patterns of tibia shaft. A, rat fed 0.3 per cent sodium fluoride; B, normal rat; C, normal rat.

In Figure 10 it can be seen that the parathormone pattern (c) is different than any of the others in that the line (1) has shifted from about 3.05 Å on the normal pattern to about 3.18 Å on the parathormone pattern, also the line (2) appears on the parathormone pattern at about 2.6 Å. Table X

figures which are characteristic of the particular pattern. No explanation can be given of this change until additional chemical analysis has been made and further work has been done on synthetic apatites and the effect of heat on natural compounds.

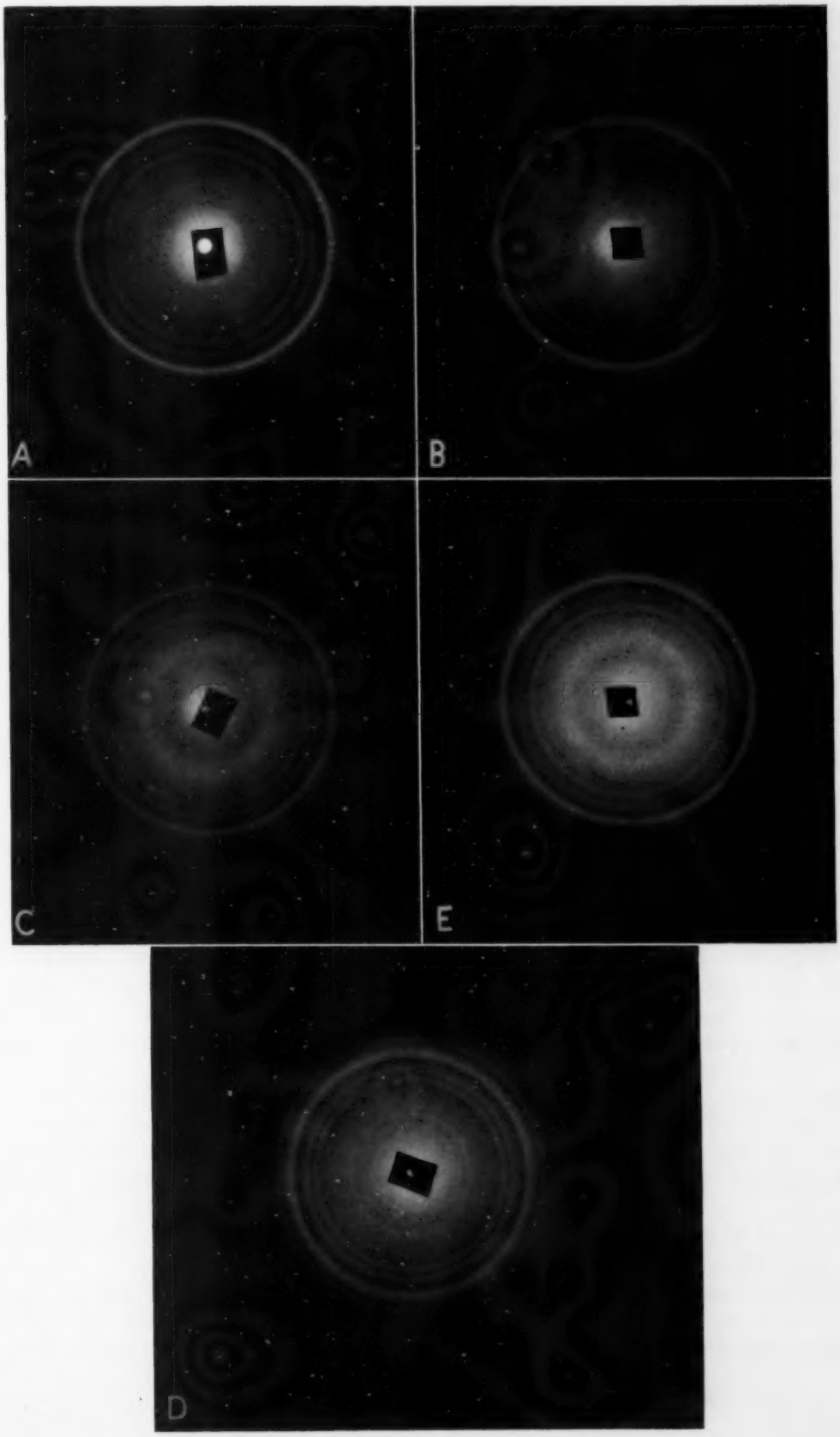

Fig. 13. Powder patterns, ashed tibia shaft. A, rachitic rat; B, C, D, E, rats injected with parathormone.

Table IX shows the chemical composition of the tibiae of the rats used in this study. The figures are averages for the various dietetic groups used. The apparent inconsistency of the amounts of fluorine, calcium and phosphorus found in the bone of the animals fed 0.1 per cent sodium fluoride and those fed 0.3 per cent is made clear by the time the treatment covered. The toxic dosage produced death in a short while but some of the rats continued indefinitely upon the smaller amount. It is interesting to note that between the fourth and sixth day after the rats consumed a sodium fluoride containing diet (either the 0.1 or 0.3 per cent NaF), there appeared a striking engorgement of the blood vessels of the ears which was more apparent with the higher intakes of sodium fluoride. Figure 10 also shows that the parathormone plus 0.3 per cent sodium fluoride (B) is the same as the normal bone and that the 0.3 per cent sodium fluoride alone (D) has practically no effect on the pattern of the ashed epiphysis. The ashed epiphysis of a rachitic rat may give either a normal pattern, Figures 11B, 11C or one like the parathormone, Figure 11A, depending upon the extent of the disease. Figure 11 shows patterns from the ashed epiphyses of rachitic rats, Figures 11B and 11C are from a rat whose serum calcium was 12.9 mg. The diagrams from the ashed shaft agree with those from the ashed epiphysis in the cases of the rats having rickets, those fed on a diet containing 0.3 per cent sodium fluoride, and those receiving the sodium fluoride plus parathormone. Figure 12A shows a 0.3 per cent sodium fluoride diagram and Figure 13A shows a architic diagram. Figures 12A and 12B are diagrams from the two tibiae of a normal rat. Those both agree with the pattern characteristic of parathormone. A possible explanation of this might be that the rat which we were using and thought was normal really possessed some signs of a pathological condition. However, in Figure 13, B, C, D and E are from rats injected with parathormone, and we note that in only one case, 13D, do we have a characteristic parathormone pattern. The patterns of the ashed main shaft of the parathormone injected rats seem to be less affected than the epiphysis and to some extent rather irregularly. Table X gives the spacing measurement in Ångströms for the normal and the parathormone rats.

Much more experimental work should be done before drawing a conclusion, however general, about the relative structure of the normal and the parathormone bone.

SUMMARY

It has been shown that:

1. Apatite structure is retained by the incisors and tibiae of rats fed fluoride diet, aluminum sulphate, or combinations of both, injected with parathormone, injected with parathormone and fed fluoride, and those which are rachitic.

2. Irregular structure was found in a varying degree in all teeth used, the greatest irregularity being in the teeth from animals fed sodium fluoride.

3. The brittleness of the fluoride teeth is due to a lack of orientation, increased crystal size and heterogeneity of the material.

4. Parathormone produces increased orientation with a crystal size which corresponds well with the normal.

5. There is practically no orientation in the epiphysis of either the normal or the pathological bones so far studied.

6. Diet which is 0.3 per cent sodium fluoride tends to increase the crystal size in the tibia.

7. Unashed bone of the normal, rachitic, parathormone, 0.3 per cent sodium fluoride and 0.3 per cent sodium fluoride and parathormone all give approximately the same reflection pattern and powder pattern, showing approximately the same chemical composition of the bone.

8. The ashed epiphysis patterns show a slight difference from the unashed in the case of the normal and parathormone rats.

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Twenty-third Annual Meeting, 1938: To be announced.

EDITORIALS

LORD RUTHERFORD OF NELSON
1871–1937

BY THE death of Lord Rutherford, which occurred on October 19, we, as radiologists, have lost not only one of the outstanding figures in the science of radiations and their application to the problems of atomic structure, but a friend, a man who, in spite of the honours heaped upon him from every quarter of the world, was still a man, a joyous, exuberant, and very human man, whose interests extended far beyond the confines of his own laboratories into many spheres, one of which was the application of radiations to medical problems.

Born in 1871 at Nelson in New Zealand, Rutherford received his early education locally and proceeded to Canterbury College at Christchurch. Here, at the age of twenty-three, he gained a scholarship that took him to England to the Cavendish Laboratory at Cambridge where he worked under J. J. Thomson. He earned a bare existence as a research student and it was the good fortune of one of the writers of this notice (A.E.B.) to be sent to him as his first pupil for private tuition. This was in 1896 and there was little to indicate that the man who was doing this hack work was on the threshold of the chain of discoveries which have placed his name high in the constellation of brilliant physicists who have enhanced the name of the Cavendish Laboratory and established for it such a wonderful prestige. One would not have foretold a brilliant achievement for the jolly, almost boisterous, fellow, who took such delight in strenuous living and making everyone about him happy, even though he had a knack of imposing his will on others.

In 1898 he left Cambridge and became Professor of Physics at McGill University, Montreal, and it was here that he did much of the fundamental work that established his reputation. Fellowship of the Royal Society came in 1903. In 1907 Rutherford returned to England as Professor of Physics at Manchester, and honours came to him one after another, including the Nobel Prize in 1908. In Manchester he took a keen interest in the initiation of the Radium Institute. It was very largely Rutherford's influence that dictated the outline of the scheme, and his advice on the technical side was freely given and greatly valued.

In 1919, on the retirement of J. J. Thomson, Rutherford returned to Cambridge as Cavendish Professor of Physics, and in the eighteen years of his administration he gathered round him a band of workers whose researches made this laboratory the Mecca of physicists. At that time the Diploma in Medical Radiology and Electrology was under discussion. Rutherford at once took an active part and offered the facilities of the Cavendish—no small thing in an already crowded laboratory. The value of this to the teaching of the Diploma students was indeed a service to radiology. In Committee he was a great force—the ready laugh behind that forceful personality disarmed criticism and put trivialities and non-essentials in their proper place. His gift for sensing the points of real importance in a discussion was sometimes almost disconcerting, but when these points were gained it was obvious that those things on which time had been wasted were relative details and were

easily settled. No matter how busy, he made his attendance at meetings of the Radiology Committee a first call on his time. For several periods he was Chairman and had much to do with the direction of policy. In recent years he laboured hard and gave considerable time in trying to dissuade the University from carrying out its decision to abandon the Cambridge Diploma. In this he felt he was handicapped by the fact that he was a physicist and could not therefore speak with authority against the opinions of the biological interests who maintained that diplomas, in general, were not in harmony with the traditions of the University and that this Diploma had served its purpose. Moreover, they did not see the need for, or the possibilities of, a department of radiology equipped to serve the biological needs of the University. On this latter idea Rutherford was very keen and he envisaged a centralised department, linked with his own, in which the applications of radiations of all kinds could be applied to the biological sciences.

In his younger days, Rutherford was interested in electric waves, and invented an ingenious magnetic detector, but his life-work was the study of radioactivity and the structure of the nucleus. He elucidated the nature of the alpha particle, first recognised the true significance of radioactive disintegration, and put forward the extremely fruitful nuclear theory of the atom, afterwards developed mathematically by Bohr. Radiologists owe a great debt of gratitude to Lord Rutherford for his work on radioactivity, which rendered gamma-ray therapy possible.

His personal qualities were such as to endear him to all who knew him. Always straightforward and direct in his dealings, always anxious to give others their due, always friendly and sympathetic, he never grudged time spent in helping his students, colleagues and friends, no matter how busy he might be. His drive was terrific; he seemed to get through as much work in a day as any other three men. He did not suffer fools gladly, but his ways of turning them down rapidly and effectively seldom gave rise to ill will. With a cheerful word for everyone, he took a personal interest in even the youngest and most humble member of his laboratory staff. A bluff manner, that sometimes alarmed those who knew him but slightly, merely served to conceal a real kindness of heart which no one who knew him could fail to recognise. His unselfishness and his gift for collaboration and advice were extraordinary—he knew and almost, if not actually, collaborated in the work of the forty or more research students who occupied every hole and corner of his laboratory. His influence was such that if he was away for more than a day he could detect a slackening on his return. As he told one of us (A.E.B.) recently, it was this that made him drive himself so hard and made it impossible for him to ease up.

The importance of Rutherford's work was recognised in the honours which were bestowed upon him: a knighthood in 1914, the Order of Merit in 1925, and a peerage in 1931. But in spite of his great achievements and the immense regard in which he was held throughout the scientific world, he remained essentially simple in his tastes, and even humble in his outlook When his name appeared in the New Year's Honours List in 1931, and he must have received thousands of greetings from all over the globe, it was characteristic of him that he answered a letter of congratulation (from G.S.) in his own hand. One sentence in that letter is worth quoting. He wrote, "It will not involve a change of name, and I hope it won't mean any change of nature either." That sentence is typical of him; nothing could or ever did change his nature.

A. E. Barclay
G. Stead

CHARLES EASTMOND
1879–1937

DR. CHARLES EASTMOND, a member of the American Roentgen Ray Society since 1906, died on November 27, 1937, exactly one month before he would have attained the age of fifty-eight. He passed through an illness lasting several years, which did not completely incapacitate him, except for short periods.

Dr. Eastmond was born in Brooklyn, N. Y., on December 27, 1879, his father, Theodore Eastmond, being of English and Old New York Dutch stock, his mother Emeline E. Farnham, of Connecticut English stock going back to 1687.

He attended public and high schools in Brooklyn, then Columbia College, receiv-

ing the degree of A.B. in 1901, and the College of Physicians and Surgeons, graduating with the degree of M.D. in 1904, the last year at Columbia College being taken as the first year at Medical School.

He began the practice of roentgenology in 1905 and had limited his work to that specialty ever since. In 1907 he did postgraduate work in roentgenology in Vienna. He has had charge of the roentgen departments of several of the important Brooklyn hospitals for many years. According to his own statement recently, he has "now as an old man been relegated to the consulting staff of some eight or nine hospitals in Brooklyn and Long Island." At the time of his death he was roentgenologist to the Carson Peck Memorial Hospital in Brooklyn.

During the war he served as a medical officer in the Navy with the rank of Lieutenant, Junior Grade, from March 1917 to April 1919; of this period, he saw seven months' service in France, the rest of the time at the Brooklyn Navy Yard and in the Brooklyn Naval Hospital.

His contributions to roentgen literature were few but important. Among these is a chapter entitled "The Uses of X-ray in Medical Diagnosis" in Butler's Diagnostic Internal Medicine, in 1910; a paper "Metastatic Thoracic Disease" in the *Long Island Medical Journal*, August 1924; and a paper entitled "Gastro-intestinal Infection; Its Roentgen Manifestations" read before the First International Congress of Radiology, London, 1925 (*British Journal of Radiology*, 1926, *31*, 93).

The latter paper is one which presented a good deal of valuable and perhaps original information. Unfortunately, Estmond was too modest and did not publicize his conclusions by repetition. Consequently, when several years later terminal ileitis was described as a clinical entity, Estmond evidently did not care, and others, including the writer who had been present at the reading of the paper, had forgotten what he had said. To quote from the paper:

> The process here (ileum) is . . . a rigidity, a lack of elasticity and an alteration of the rate at which the barium passes through the part. On the X-ray films there may be a full-calibred intestine with the rugae flattened out so as to present a smooth-walled margin, or later in the history of the condition an irregularity of form more or less constant and diminution of the size of the lumen from contracture. This contracture like those higher in the tract is not affected by the use of antispasmodics. The condition is not one of spasm but one of congestion with small round-cell infiltration, fibrosis and more or less cicatricial narrowing.

The entire paper is worth re-reading, especially in the light of subsequent events.

He was an active member on the Committee which organized the participation of American Radiologists in the First International Congress of Radiology in London, at which he himself presented the paper referred to.

A great deal of his work was that of expert in court. On one occasion we met on the opposite sides of a case on trial. He impressed me then with the integrity of his conception of his duties as an expert; what I have later on heard from others, has convinced me of his honesty and unswerving devotion to truth.

In character and ability he was one of the outstanding radiologists in the metropolitan district of New York, and by his personal charm and sympathetic nature he made many friends among his colleagues and his patients. Like many radiologists, he was an enthusiastic golfer.

He was always cheerful, and even during his last months, when he had periods of severe pain and discomfort, he never lost his sense of humor. He never practised pretense, he never attitudinized but he always was human and natural.

Among those of us who knew him, he leaves only the fondest of memories, and to the writer, his passing has left a void which is not soon to be filled.

Leopold Jaches

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. B. Peirce, University Hospital. Ann Arbor, Mich. Annual Meeting: Atlantic City, Sept. 20–23, 1938.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting, 1938: To be announced.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: San Francisco, Calif., June 13–17, 1938.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1938: To be announced.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY
Secretary, Dr. Howard H. Ashbury, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Special meetings may be called by the Chairman.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, Dr. M. L. Pindell, 678 S. Ferris Ave., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. North W. Shetter, 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. E. A. Schmidt, 4200 E. 9th Ave., Denver, Colo. Meets third Tuesday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Harold O. Brown, Tampa, Florida. Meetings held twice a year, May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets twice annually: in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. S. G. Schenck, 115 Eastern Parkway, Brooklyn, N. Y. Meets at Kings County Med. Soc. Bldg. on third Thursday of each month from October to May, at 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

NEBRASKA RADIOLOGICAL SCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. H. K. Taylor, 667 Madison Ave., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Two day annual meeting, May, 1938. Exact date and place to be decided.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. H. N. Mawhinney, Mercy Hospital. Two fall and two spring meetings—time and place designated by the president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Fran.

*Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

cisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina Medical Assn.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. M. H. Glover, 414 Hamilton Bldg., Wichita Falls, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich. Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section on Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson, Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

DIPLOMATES AMERICAN BOARD OF RADIOLOGY

The following is a list of diplomates of The American Board of Radiology:

1. ABBOTT, HODSON A., New York, N. Y., *Radiology*.
2. ABERCROMBIE, EUGENE, Knoxville, Tenn., *Roentgenology*.
3. ABOWITZ, JACOB, Los Angeles, Cal., *Roentgenology*.
4. ABRAHAM, ARDEN L., Minneapolis, Minn., *Radiology*.
5. ACHILLES, WILLIAM E., Geneva, N. Y., *Diagnostic Roentgenology*.
6. ACKEMANN, H. W., Rockford, Ill., *Radiology*.
7. ADAIR, FRANK E., New York, N. Y., *Therapeutic Radiology*.
8. ALBERT, SIMON, Providence, R. I., *Radiology*.
9. ALEXANDER, F. K., Philadelphia, Pa., *Radiology*.
10. ALGIN, SERGIUS V., Indiana, Pa., *Diagnostic Roentgenology*.
11. ALLEN, B. M., Wilmington, Del., *Diagnostic Roentgenology*.
*12. ALLEN, BUNDY, Tampa, Fla., *Radiology*.
13. ALLEN, KENNETH D. A., Denver, Colo., *Radiology*.
14. ALLEN, LEWIS G., Kansas City, Kans., *Radiology*.
15. ALLEN, M. LOWRY, Philadelphia, Pa., *Radiology*.
16. ALLEN, WILLIAM E., JR., St. Louis, Mo., *Roentgenology*.
17. ALLEY, REUBEN G., Pittsburgh, Pa., *Diagnostic Roentgenology*.
18. ALLISON, R. G., Minneapolis, Minn., *Roentgenology*.
19. ALTMAN, W. S., Quincy, Mass., *Radiology*.
20. AMES, FOREST B., Bangor, Me., *Roentgenology*.
21. ANDERSON, W. D., Memphis, Tenn., *Roentgenology*.
22. ANDREWS, J. ROBERT, Cleveland, O., *Radiology*.
23. ANÉ, J. N., New Orleans, La., *Radiology*.
24. ANSPACH, WILLIAM E., Chicago, Ill., *Roentgenology*.
25. ARCHER, VINCENT W., University, Va., *Roentgenology*.
26. ARENS, ROBERT A., Chicago, Ill., *Radiology*.
27. ARNESON, A. N., St. Louis, Mo., *Therapeutic Radiology*.
28. ASHBURY, HOWARD E., Baltimore, Md., *Radiology*.
29. ASPRAY, JOSEPH M., Spokane, Wash., *Radiology*.
30. ATKINS, S. M., Waterbury, Conn., *Roentgenology*.
31. AURELIUS, J. RICHARDS, St. Paul, Minn., *Roentgenology*.
32. AVERY, PHILIP S., New Brunswick, N. J., *Roentgenology*.
33. BACHMAN, M. H., Youngstown, O., *Roentgenology*.
34. BACON, RALPH D., Erie, Pa., *Radiology*.
35. BADER, E. R., Cincinnati, O., *Radiology*.
36. BAILEY, C. O., Los Angeles, Cal., *Therapeutic Radiology*.
37. BAILEY, WILBUR, Los Angeles, Cal., *Radiology*.
38. BAIRD, JOSEPH C., Eau Claire, Wis., *Roentgenology*.
39. BAKER, CHARLES F., Newark, N. J., *Roentgenology*.
40. BAKER, EDGAR C., Youngstown, O., *Radiology*.
41. BALL, CLARENCE F., Rutland, Vt., *Therapeutic Radiology*.
42. BALL, ROBERT P., New York, N. Y., *Roentgenology*.
43. BARFIELD-CARTER, M., Birmingham, Ala., *Roentgenology*.
44. BARKER, WALTER C., Philadelphia, Pa., *Radiology*.
45. BARKER, W. ALLEN, Petersburg, Va., *Roentgenology*.
46. BARNES, JOHN M., Buffalo, N. Y., *Roentgenology*.
47. BARNETT, ARTHUR F., Eugene, Ore., *Radiology*.
48. BARR, RICHARD E., Beaumont, Tex., *Therapeutid Radiology*.
49. BARROW, S. C., Shreveport, La., *Radiology*.
50. BARTH, EARL E., Chicago, Ill., *Roentgenology*.
51. BATCHELDER, PHILIP, Providence, R. I., *Roentgenology*.
52. BAUER, AUGUST A., Chicago, Ill., *Roentgenology*.
53. BAUM, SAMUEL M., New York, N. Y., *Therapeutic Radiology*.
54. BAXTER, O. D., Sumter, S. C., *Radiology*.
55. BEALS, JOHN A., Greenville, Miss., *Radiology*.
56. BEELER, RAYMOND C., Indianapolis, Ind., *Radiology*.
57. BEILIN, D. S., Chicago, Ill., *Radiology*.
58. BELL, A. L. L., Brooklyn, N. Y., *Roentgenology*.
59. BELL, J. SHERIDAN, Waterbury, Conn., *Diagnostic Roentgenology*.
60. BELL, JOSEPH C., Louisville, Ky., *Roentgenology*.
61. BENDICK, ARTHUR J., New York, N. Y., *Radiology*.
*62. BENISHEK, WERNER L., Aurora, Ill., *Roentgenology*.
63. BENJAMIN, EMANUEL W., Providence, R. I., *Radiology*.
64. BENNETT, JAMES P., Chicago, Ill., *Roentgenology*.
65. BERG, H. MILTON, Bismarck, N. D., *Radiology*.
66. BERGER, RAYMOND A., Richmond, Va., *Radiology*.
67. BERNATH, GERALD J., Detroit, Mich., *Diagnostic Roentgenology*.
68. BERNSTEIN, J. H., New York, N. Y., *Radiology*.
69. BERTIN, E. J., Philadelphia, Pa., *Roentgenology*.
70. BESSER, HERMAN, New York, N. Y., *Radiology*.
71. BETHEA, W. R., Memphis, Tenn., *Roentgenology*.
*72. BETTS, ARTHUR, Spokane, Wash., *Radiology*.
73. BIRSDALL, EDGAR, Glens Falls, N. Y., *Roentgenology*.
74. BIRKBECK, NORMAN J., Dayton, O., *Radiology*.
75. BIRKELO, C. C., Detroit, Mich., *Roentgenology*.
76. BISHOP, PAUL A., Philadelphia, Pa., *Radiology*.
77. BLACKETT, CHARLES W., Boston, Mass., *Roentgenology*.
78. BLAINE, EDWARD S., Los Angeles, Cal., *Roentgenology*.
79. BLAKE, HENRY K., New York, N. Y., *Roentgenology*.
80. BLAKE, T. W., Rochester, Minn., *Radiology*.
81. BLISS, GERALD D., Altoona, Pa., *Radiology*.
82. BLOOM, ARTHUR R., Detroit, Mich., *Roentgenology*.
83. BOGAN, ISABEL K., Brookline, Mass., *Roentgenology*.
84. BOGAN, MARY E., Brookline, Mass., *Roentgenology*.
85. BOGART, FRANKLIN B., Chattanooga, Tenn., *Roentgenology*.
86. BOICE, RALPH H., Parkersburg, W. Va., *Radiology*.
87. BONNAR, JAMES M., New Bedford, Mass., *Radiology*.
88. BONOFF, KARL M., Los Angeles, Cal., *Diagnostic Roentgenology*.
89. BOONE, WILLIAM H., New York, N. Y., *Roentgenology*.
90. BORMAN, C. H., Minneapolis, Minn., *Radiology*.
91. BORRELLI, FRANK J., New York, N. Y., *Diagnostic Roentgenology*.
92. BORZELL, F. F., Philadelphia, Pa., *Radiology*.
93. BOUSLOG, JOHN S., Denver, Colo., *Radiology*.
94. BOVARD, PAUL G., Tarentum, Pa., *Diagnostic Roentgenology*.
95. BOWEN, CARL B., Oakland, Cal., *Roentgenology*.
96. BOWEN, David R., Philadelphia, Pa., *Radiology*.
97. BOWIE, E. R., New Orleans, La., *Roentgenology*.
98. BOWING, HARRY H., Rochester, Minn., *Therapeutic Radiology*.
99. BOYD, JAMES F., Providence, R. I., *Radiology*.
100. BOYES, JAMES G., Plainfield, N. J., *Roentgenology*.
101. BRADLEY, ROBERT A., Atlantic City, N. J., *Radiology*.
102. BRAMS, JULIUS, Chicago, Ill., *Radiology*.
103. BRANDENBURG, H. P., Denver, Colo., *Radiology*.
104. BRAUN, BENJ. D., Chicago, Ill., *Radiology*.
105. BRENNAN, FRANCIS J., Oshkosh, Wis., *Diagnostic Roentgenology*.
106. BRENNEMAN, R. E., Meadville, Pa., *Radiology*.
107. BRIDENBAUGH, J. H., Billings, Mont., *Radiology*.
108. BRITTAIN, OMAN R., Salina, Kans., *Roentgenology*.
109. BROESER, HENRY V., Hoboken, N. J., *Diagnostic Roentgenology*.
110. BROMER, RALPH S., Bryn Mawr, Pa., *Radiology*.
111. BROOKSHER, W. R., Fort Smith, Ark., *Radiology*.
112. BROUSE, IVAN E., Jacksonville, Ill., *Roentgenology*.
113. BROWN, H. O., Tampa, Fla., *Roentgenology*.
114. BROWN, PERCY, Boston, Mass., *Roentgenology*.
115. BROWN, SAMUEL, Cincinnati, O., *Roentgenology*.
116. BRUCK, SAMUEL, Philadelphia, Pa., *Radiology*.
117. BRYAN, LLOYD, San Francisco, Cal., *Roentgenology*.
118. BURCH, HOBART A., Elmira, N. Y., *Radiology*.
119. BURCHAM, THOMAS A., Des Moines, Ia., *Radiology*.
120. BURDICK, MITCHELL, Erie, Pa., *Roentgenology*.
121. BURGESS, CHARLES J., Lawrence, Mass., *Radiology*.
122. BURNETT, H. W., Dayton, O., *Roentgenology*.
123. BUTLER, NICHOLAS G., Hartford, Conn., *Radiology*.
124. BUTLER, P. F., Boston, Mass., *Radiology*.
125. CALDWELL, CHARLES S., Pittsburgh, Pa., *Roentgenology*.
126. CALLEN, HAROLD S., Bradford, Pa., *Radiology*.

127. Camp, John D., Rochester, Minn., *Roentgenology.*
128. Campbell, Lloyd A., Saginaw, Mich., *Therapeutic Radiology.*
129. Capp, Charles S., San Francisco, Cal., *Radiology.*
130. Carlson, Glenn D., Dallas, Tex., *Roentgenology.*
131. Carr, Edson W., Chicago, Ill., *Diagnostic Roentgenology.*
132. Carter, Ray A., Los Angeles, Cal., *Roentgenology.*
133. Carty, John R., New York, N. Y., *Radiology.*
134. Case, James T., Chicago, Ill., *Radiology.*
135. Cassidy, Raymond M., Chicago, Ill., *Roentgenology.*
136. Cathcart, John W., El Paso, Tex., *Radiology.*
137. Challenger, Chester J., Chicago, Ill., *Roentgenology.*
138. Chamberlain, W. Edward, Philadelphia, Pa., *Radiology.*
139. Chamberlin, George W., Philadelphia, Pa., *Radiology.*
140. Chapman, John F., Pasadena, Cal., *Roentgenology.*
141. Childe, Arthur E., Montreal, Que., *Diagnostic Roentgenology.*
142. Childs, D. S., Syracuse, N. Y., *Roentgenology.*
143. Childs, S. B., Denver, Colo., *Roentgenology.*
144. Chilko, A. J., New Rochelle, N. Y., *Roentgenology.*
145. Christie, Arthur C., Washington, D. C., *Radiology.*
146. Church, John E., Pontiac, Mich., *Roentgenology.*
147. Cilley, Earl I. L., Bellingham, Wash., *Radiology.*
148. Claiborne, E. M., New York, N. Y., *Radiology.*
149. Clapp, Roland D., West Medford, Mass., *Radiology.*
150. Clark, D. M., Santa Barbara, Cal., *Radiology.*
151. Clark, James J., Atlanta, Ga., *Roentgenology.*
152. Clark, Stanley A., South Bend, Ind., *Radiology.*
153. Clark, William T., Janesville, Wis., *Radiology.*
154. Clarkson, Wright, Petersburg, Va., *Radiology.*
155. Cleaves, Edwin N., Boston, Mass., *Diagnostic Roentgenology.*
156. Cleghorn, Charles D., Miami, Fla., *Radiology.*
157. Clement, Gage, Duluth, Minn., *Radiology.*
158. Cleveland, W. R., Evansville, Ind., *Radiology.*
159. Climan, Max, Hartford, Conn., *Diagnostic Roentgenology.*
160. Coate, J. D., Oakland, Cal., *Radiology.*
161. Coe, Fred O., Washington, D. C., *Radiology.*
162. Coffin, Whitman K., Boston, Mass., *Roentgenology.*
163. Cohoon, Carl W., Bay Shore, N. Y., *Diagnostic Roentgenology.*
164. Colcher, A. Edward, Philadelphia, Pa., *Diagnostic Roentgenology.*
165. Cole, J. M., Windsor, Ont., *Roentgenology.*
166. Cole, Lewis Gregory, New York, N. Y., *Roentgenology.*
167. Cole, Paul F., Springfield, Mo., *Radiology.*
168. Cole, William Gregory, New York, N. Y., *Roentgenology.*
169. Coley, Stephen W., Memphis, Tenn., *Roengtenology.*
170. Colgan, William S., Bridgeport, Pa., *Radiology.*
171. Collins, E. R., Cleveland, O., *Diagnostic Roentgenology.*
172. Collins, James N., Indianapolis, Ind., *Radiology.*
173. Collins, John J., Thomasville, Ga., *Radiology.*
174. Cook, Benjamin F., Rutland, Vt., *Diagnostic Roentgenology.*
175. Cook, Carroll E., Chicago, Ill., *Diagnostic Roentgenology.*
176. Cook, Orrin S., Sacramento, Cal., *Roentgenology.*
177. Cook, Philip H., Worcester, Mass., *Radiology.*
178. Cooley, R. M., Jackson, Mich., *Roentgenology.*
179. Copleman, Benjamin, Perth Amboy, N. J., *Radiology.*
180. Coray, Q. R., Salt Lake City, Utah, *Roentgenology.*
181. Corcoran, William J., Scranton, Pa., *Roentgenology.*
182. Cornett, George W., Yakima, Wash., *Roentgenology.*
183. Costolow, William E., Los Angeles, Cal., *Therapeutic Radiology.*
184. Covington, E. Eugene, Baltimore, Md., *Therapeutic Radiology.*
185. Cowan, Irving I., Milwaukee, Wis., *Diagnostic Roentgenology.*
186. Cowherd, Frank G., Cumberland, Md., *Roentgenology.*
187. Cox, Michael J., Pittsfield, Mass., *Roentgenology.*
188. Crain, C. F., Corpus Christi, Tex., *Radiology.*
189. Cramp, G. W., Brooklyn, N. Y., *Roentgenology.*
*190. Crane, A. W., Kalamazoo, Mich., *Roentgenology.*
191. Crawford, Helen L., Indianapolis, Ind., *Roentgenology.*
192. Crosby, Leonard G., Denver, Colo., *Radiology.*
193. Crossan, John W., Los Angeles, Cal., *Diagnostic Roentgenology.*
194. Crowder, E. R., Evanston, Ill., *Roentgenology.*
195. Cummings, Edson S., Portland, Me., *Roentgenology.*
196. Cunningham, Lester W., Mandarin, Fla., *Roentgenology.*
197. Currin, Francis W., Brooklyn, N. Y., *Roentgenology.*
198. Curtis, Richard C., Corsicana, Tex., *Diagnostic Roentgenology.*
199. Cushway, B. C., Chicago, Ill., *Radiology.*
200. D'Amico, Michael, New Haven, Conn., *Roentgenology.*
201. Dahl, H. W., Des Maines, Ia., *Diagnostic Roentgenology.*
202. Dann, David S., Kansas City, Mo., *Radiology.*
203. Dannenberg, Max, Brooklyn, N. Y., *Roentgenology.*
204. Danzer, Joseph T., Oil City, Pa., *Radiology.*
205. Dauksys, Joseph, Excelsior Springs, Mo., *Diagnostic Roentgenology.*
206. Davidson, S. G., Bluefield, W. Va., *Roentgenology.*
207. Davidson, Sol C., Rochester, N. Y., *Roentgenology.*
208. Davis, Ernest L., Springfield, Mass., *Roentgenology.*
209. Davis, F. M., San Antonio, Tex., *Diagnostic Roentgenology.*
210. Davis, H. E., Chicago, Ill., *Radiology.*
211. Davis, Henry B., Lancaster, Pa., *Radiology.*
212. Davis, Kenneth S., Los Angeles, Cal., *Roentgenology.*
213. Davison, C. O., Poughkeepsie, N. Y., *Radiology.*
214. Davison, R. Winthrop, Trenton, N. J., *Roentgenology.*
215. Debbie, Anthony G., St. Albans, N. Y., *Diagnostic Roentgenology.*
216. Decker, Fred H., Peoria, Ill., *Radiology.*
217. Deetjen, Christian, Baltimore, Md., *Radiology.*
218. DeGraff, Ralph M., Buffalo, N. Y., *Diagnostic Roentgenology.*
219. DeHollander, William, Springfield, Ill., *Roentgenology.*
220. deLorimier, Alfred A., Ancon, Canal Zone, *Radiology.*
221. Delario, Anthony J., Patterson, N. J., *Radiology.*
222. Dempster, J. H., Detroit, Mich., *Diagnostic Roentgenology.*
223. Denham, Harry C., Gloversville, N. Y., *Diagnostic Roentgenology.*
224. Derr, John S., Frederick, Md., *Roentgenology.*
225. Desjardins, Anatole, Wilkes-Barre, Pa., *Roentgenology.*
226. Desjardins, Arthur U., Rochester, Minn., *Radiology.*
227. Dessen, Edward, Philadelphia, Pa., *Radiology.*
228. Dessen, Louis A., Hazelton, Pa., *Diagnostic Roentgenology.*
229. Deweese, E. R., Kansas City, Mo., *Radiology.*
230. Dick, Paul G., Chicago, Ill., *Roentgenology.*
231. Dickinson, J. G., Tampa, Fla., *Roentgenology.*
232. Dixon, George S., New York, N. Y., *Diagnostic Roentgenology.*
233. Donaldson, S. W., Ann Arbor, Mich., *Roentgenology.*
234. Doub, Howard P., Detroit, Mich., *Radiology.*
235. Doughty, William M., Cincinnati, O., *Radiology.*
236. Dowell, Dawson A., Omaha, Neb., *Radiology.*
237. Downing, Robert E., Terre Haute, Ind., *Radiology.*
238. Downs, Elwood E., Woodbury, N. J., *Radiology.*
239. Drane, Robert, Savannah, Ga., *Roentgenology.*
240. Dresser, Richard, Boston, Mass., *Radiology.*
241. Duckworth, Roy D., White Plains, N. Y., *Roentgenology.*
242. Duckworth, Willard D., New Rochelle, N. Y., *Roentgenology.*
243. Duffy, James J., New York, N. Y., *Therapeutic Radiology.*
244. Dumas, Charles E., Worcester, Mass., *Radiology.*
245. Dunham, H. Kennon, Cincinnati, O., *Diagnostic Roentgenology.*
246. Durrance, Fred Y., Houston, Tex., *Roentgenology.*
247. Dyke, Cornelius G., New York, N. Y., *Roentgenology.*
248. Eastland, William E., Oklahoma City, Okla., *Therapeutic Radiology.*
*249. Eastmond, Charles, Brooklyn, N. Y., *Roentgenology.*
250. Edeiken, Louis, Philadelphia, Pa., *Radiology.*
251. Edstrom, Henry, Dubuque, Ia., *Radiology.*

252. EDWARDS, HAROLD G. F., Shreveport, La., *Radiology*.
253. EDWARDS, J. BENNETT, Englewood, N. J., *Roentgenology*.
254. EGBERT, W. E., Chester, Pa., *Diagnostic Roentgenology*.
255. EHRENPREIS, BERNARD, Brooklyn, N. Y., *Roentgenology*.
256. EHRLICH, DAVID E., New York, N. Y., *Radiology*.
257. EISEN, DAVID, Toronto, Ont., *Diagnostic Roentgenology*.
258. ELDRIGE, WATSON W., JR., Washington, D. C., *Roentgenology*.
259. ELEY, CALYTON W., Norfolk, Va., *Roentgenology*.
260. ELLIOTT, FREDERIC E., Brooklyn, N. Y., *Radiology*.
261. ELLIS, IVAN G., Madison, Wis., *Roentgenology*.
262. ELWARD, JOSEPH F., Washington, D. C., *Roentgenology*.
263. ENEBOE, JOHN B., San Diego, Cal., *Radiology*.
264. ENFIELD, CHARLES D., Louisville, Ky., *Radiology*.
265. ERICKSEN, LESTER G., South Bend, Ind., *Radiology*.
266. ERNST, EDWIN C., St. Louis, Mo., *Radiology*.
267. ERSKINE, ARTHUR W., Cedar Rapids, Ia., *Radiology*.
268. ETTINGER, ALICE, Boston, Mass., *Diagnostic Roentgenology*.
269. EVANS, HARRY D., Philadelphia, Pa., *Diagnostic Roentgenology*.
270. EVANS, JOHN, Baltimore, Md., *Roentgenology*.
271. EVANS, WILLIAM A., Detroit, Mich., *Radiology*.
272. EVELETH, FRED S., Concord, N. H., *Roentgenology*.
273. EXNER, FREDERICK B., Seattle, Wash., *Radiology*.

274. FARMER, HARRY L., Cleveland, O., *Radiology*.
275. FARRELL, JOHN T., JR., Philadelphia, Pa., *Roentgenology*.
276. FAUST, J. J., Tyler, Tex., *Radiology*.
277. FAVOUR, RICHMOND, JR., Washington, D. C., *Radiology*.
278. FEASTER, O. O., St. Petersburg, Fla., *Radiology*.
279. FERGUSON, JAMES W., Pittsburgh, Pa., *Radiology*.
280. FEUERSTEIN, BENJAMIN L., Bay Shore, N. Y., *Therapeutic Radiology*.
281. FINEMAN, SOLOMON, New York, N. Y., *Roentgenology*.
282. FINKELSTEIN, ARTHUR, Philadelphia, Pa., *Radiology*.
283. FINNEGAN, JAMES F., Portsmouth, Va., *Roentgenology*.
284. FINNEY, GUY A., Topeka, Kans., *Diagnostic Roentgenology*.
285. FIROR, WHITMER B., Baltimore, Md., *Radiology*.
286. FISHER, J. W., Pittsburgh, Pa., *Radiology*.
287. FISHER, L. F., South Bend, Ind., *Roentgenology*.
288. FLAX, NATHAN, Cincinnati, O., *Roentgenology*.
289. FLINN, F., Decatur, Ill., *Radiology*.
290. FLIPPIN, EUGENE L., Baltimore, Md., *Radiology*.
291. FLYNN, JAMES M., Rochester, N. Y., *Radiology*.
292. FOLEY, JOSEPH M., Peoria, Ill., *Roentgenology*.
293. FOLKINS, FRANK H., Redlands, Cal., *Roentgenology*.
294. FORD, FRANCES A., Detroit, Mich., *Radiology*.
295. FORT, W. A., Mare Island, Cal., *Roentgenology*.
296. FORTIER, LUCIEN A., New Orleans, La., *Radiology*.
297. FOUTS, ROY W., Omaha, Neb., *Roentgenology*.
298. FRANCIS, HERBERT C., Nashville, Tenn., *Roentgenology*.
299. FRANK, CHARLES H., Batavia, N. Y., *Diagnostic Roentgenology*.
300. FRAY, WALTER W., Rochester, N. Y., *Radiology*.
301. FREEDMAN, EUGENE, Cleveland, O., *Roentgenology*.
302. FREEDMAN, JOHN, Detroit, Mich., *Roentgenology*.
303. FREID, JACOB R., New York, N. Y., *Radiology*.
304. FRENCH, GORDAN S., London, Ont., *Radiology*.
305. FRERE, JOHN M., Chattanooga, Tenn., *Roentgenology*.
306. FRICKE, ROBERT E., Rochester, Minn., *Therapeutic Radiology*.
307. FRIEDLAND, HENRY, New York, N. Y., *Diagnostic Roentgenology*.
308. FRIEDMAN, ASA B., Brooklyn, N. Y., *Radiology*.
309. FRIEDMAN, HARRY F., Boston, Mass., *Radiology*.
310. FREEMAN, JACQUES, Bradford, Pa., *Roentgenology*.
311. FRIEDMAN, LEWIS J., New York, N. Y., *Diagnostic Roentgenology*.
312. FRIEDMAN, MAX, New York, N. Y., *Diagnostic Roentgenology*.
313. FRIEDMAN, MILTON, Newark, N. J. *Therapeutic Radiology*.
314. FRIEDMAN, MURRAY M., New York, N. Y., *Radiology*.
315. FRUCHTER, JOSEPH M., Philadelphia, Pa., *Radiology*.
316. FUGATE, ISAAC T., Louisville, Ky., *Radiology*.
317. FULMER, CHARLES C., San Francisco, Cal., *Roentgenology*.
318. FULTON, HUSTON F., Columbus, O., *Diagnostic Roentgenology*.
319. FUREY, WARREN W., Chicago, Ill., *Radiology*.
320. FURST, NATHAN J., Newark, N. J., *Diagnostic Roentgenology*.

321. GALANTI, CHARLES P., Chicago, Ill., *Roentgenology*.
322. GARLAND, L. H., San Francisco, Cal., *Radiology*.
323. GARRETT, LESLIE M., Eau Claire, Wis., *Radiology*.
324. GATELY, TRACY T., New Orleans, La., *Radiology*.
325. GATES, RUSSELL, Minto, N. D., *Roentgenology*.
326. GELEHRTER, JOSEPH, Philadelphia, Pa., *Radiology*.
327. GEMMELE, J. H., Rochester, Pa., *Roentgenology*.
328. GEORGE, ARIAL W., Boston, Mass., *Roentgenology*.
329. GERBER, ISAAC, Providence, R. I., *Radiology*.
330. GERSHON-COHEN, JACOB, Philadelphia, Pa., *Radiology*.
331. GEYMAN, MILTON J., Santa Barbara, Cal., *Diagnostic Roentgenology*.
332. GHRIST, DAVID M., Glendale, Cal., *Roentgenology*.
333. GIAN-FRANCESCHI, JOSEPH, Buffalo, N. Y., *Diagnostic Roentgenology*.
334. GIANTURCO, CESARE, Urbana, Ill., *Roentgenology*.
335. GILES, ROY G., San Antonio, Tex., *Roentgenology*.
336. GILLIES, CARL L., Cedar Rapids, Ia., *Radiology*.
337. GILMORE, W. M., Stratford, Ont., *Radiology*.
338. GINGOLD, JOSEPH R., Meadville, Pa., *Roentgenology*.
339. GLOVER, M. H., Wichita Falls, Tex., *Radiology*.
340. GOIN, LOWELL S., Los Angeles, Cal., *Roentgenology*.
341. GOLDEN, ROSS, New York, N. Y., *Roentgenology*.
342. GOLDMAN, LEONARD B., Jamaica, L. I., N. Y., *Therapeutic Radiology*.
343. GOLDSMITH, MAURICE F., Pittsburgh, Pa., *Roentgenology*.
344. GOLDSTONE, KARL H., West New York, N. J., *Roentgenology*.
345. GOODMAN, MOSES, Brooklyn, N. Y., *Radiology*.
346. GOODRICH, MURRAY E., Toledo, O., *Radiology*.
347. GOODWIN, PERRY B., Peoria, Ill., *Radiology*.
348. GORDON, DONALD C., Scranton, Pa., *Radiology*.
349. GORFINKELL, JULIUS, Pittsburgh, Pa., *Diagnostic Roentgenology*.
350. GORSLINE, CLARENCE S., Battle Creek, Mich., *Roentgenology*.
351. GOTTLIEB, CHARLES, New York, N. Y., *Diagnostic Roentgenology*.
352. GRACE, JOSEPH M., Eloise, Mich., *Radiology*.
353. GRADY, HENRY W., Washington, D. C., *Radiology*.
354. GRAHAM, RALPH S., Sacramento, Cal., *Radiology*.
355. GRANGER, AMÉDÉE, New Orleans, La., *Radiology*.
356. GRAY, HORACE D., Memphis, Tenn., *Radiology*.
357. GREEN, JOSEPH H., Rochester, N. Y., *Roentgenology*.
358. GREENBERG, DAVID S., Steubenville, O., *Roentgenology*.
359. GREENBERGER, EDWARD D., McAlester, Okla., *Radiology*.
360. GREENFIELD, HENRY, Brooklyn, N. Y., *Radiology*.
361. GRIER, G. W., Pittsburgh, Pa., *Radiology*.
362. GRIMM, HOMER W., Pittsburgh, Pa., *Therapeutic Radiology*.
363. GROARK, OWEN J., Bridgeport, Conn., *Diagnostic Roentgenology*.
364. GROESCHEL, L. B., New York, N. Y., *Radiology*.
365. GROH, JEAN A., Cleveland, O., *Roentgenology*.
366. GROOVER, THOMAS A., Washington, D. C., *Radiology*.
367. GRUBBE, EMIL H., Chicago, Ill., *Therapeutic Roentgenology*.

368. HABBE, J. EDWIN, Milwaukee, Wis., *Roentgenology*.
369. HACKLER, ROBERT H., JR., Washington, N. C., *Roentgenology*.
370. HACKNEY, URBAN P., Dallas, Tex., *Radiology*.
371. HADLEY, LEE A., Syracuse, N. Y., *Roentgenology*.
372. HALL, E. WALTER, Detroit, Mich., *Radiology*.
373. HALL, ROBERT C., Utica, N. Y., *Roentgenology*.
374. HALL, WENDELL C., Philadelphia, Pa., *Radiology*.
375. HALLEY, EDMUND P., Decatur, Ill., *Radiology*.
376. HAMILTON, CHARLES M., Nashville, Tenn., *Radiology*.

377. Hamilton, W. S., San Antonio, Tex., *Diagnostic Roentgenology.*
378. Hampton, A. O., Boston, Mass., *Radiology.*
379. Hankins, John L., Johnson City, Tenn., *Roentgenology.*
380. Hansen, Cyrus O., Minneapolis, Minn., *Radiology.*
381. Harding, D. B., Lexington, Ky., *Radiology.*
382. Hardy, Clyde C., Omaha, Neb., *Diagnostic Roentgenology.*
383. Hare, Hugh F., Boston, Mass., *Radiology.*
384. Harrell, Henry C., Texarkana, Tex., *Roentgenology.*
385. Harrington, B. D., Tacoma, Wash., *Radiology.*
386. Harrington, Leo A., Brooklyn, N. Y., *Diagnostic Roentgenology.*
387. Harris, Clarence P., Houston, Tex., *Roentgenology.*
388. Harris, John H., Harrisburg, Pa., *Radiology.*
389. Harris, Milo T., Spokane, Wash., *Radiology.*
390. Harris, T. T., Omaha, Neb., *Radiology.*
391. Harris, William, New York, N. Y., *Therapeutic Radiology.*
392. Hart, William E., Long Beach, Cal., *Diagnostic Roentgenology.*
393. Hartung, Adolph, Chicago, Ill., *Roentgenology.*
394. Hasley, Clyde K., Detroit, Mich., *Radiology.*
395. Hatchette, Stakely F., Lake Charles, La., *Radiology.*
396. Hauser, Harry, Cleveland, O., *Radiology.*
397. Hawley, Sydney J., Danville, Pa., *Roentgenology.*
398. Haworth, Wallace, Portland, Ore., *Radiology.*
399. Hay, Percy D., Jr., Florence, S. C., *Radiology.*
400. Heacock, Charles H., Memphis, Tenn., *Roentgenology.*
401. Healy, Thomas R., Boston, Mass., *Roentgenology.*
402. Heatley, John E., Oklahoma City, Okla., *Diagnostic Roentgenology.*
403. Heberding, John, Youngstown, O., *Radiology.*
404. Hefke, Hans W., Milwaukee, Wis., *Radiology.*
405. Helminiak, Mesco J., Buffalo, N. Y., *Diagnostic Roentgenology.*
406. Henderson, Samuel G., Pittsburgh, Pa., *Radiology.*
407. Hendricks, Elliott M., Fort Lauderdale, Fla., *Roentgenology.*
408. Hendrickson, Anna R., Canton, O., *Roentgenology.*
409. Henle, Carye-Belle, Newark, N. J., *Roentgenology.*
410. Henry, Lucas S., Syracuse, N. Y., *Roentgenology.*
411. Herpel, Frederick K., West Palm Beach, Fla., *Roentgenology.*
412. Herrman, W. G., Asbury Park, N. J., *Radiology.*
413. Herscher, Harry, Hines, Ill., *Radiology.*
414. Hess, George H., Uniontown, Pa., *Roentgenology.*
415. Heylmun, Harry H., Long Beach, Cal., *Diagnostic Roentgenology.*
416. Hildreth, R. C., Kalamazoo, Mich., *Radiology.*
417. Hill, Harold A., San Francisco, Cal., *Radiology.*
418. Hill, Walter C., Cleveland, O., *Roentgenology.*
419. Hilt, Lawrence M., Grank Rapids, Mich., *Roentgenology.*
420. Hilton, James M., Klamath Falls, Ore., *Roentgenology.*
421. Hirsch, I. Seth, New York, N. Y., *Radiology.*
422. Hocker, Alfred F., New York, N. Y., *Therapeutic Radiology.*
423. Hodes, Philip J., Philadelphia, Pa., *Radiology.*
424. Hodges, Fred J., Ann Arbor, Mich., *Radiology.*
425. Hodges, Fred M., Richmond, Va., *Radiology.*
426. Hodges, Paul C., Chicago, Ill., *Radiology.*
427. Hoffman, William J., New York, N. Y., *Therapeutic Radiology.*
428. Hoffmeier, Frank N., Hagerstown, Md., *Diagnostic Roentgenology.*
429. Holly, Leland E., Muskegon, Mich., *Roentgenology.*
430. Holmes, George W., Boston, Mass., *Radiology.*
431. Holmes, L. P., Augusta, Ga., *Roentgenology.*
432. Holmes, Ralph W., Chillicothe, O., *Roentgenology.*
433. Holston, Joel D., Massillon, O., *Roentgenology.*
434. Holt, William, Portland, Me., *Radium Therapy.*
435. Hopkirk, C. C., Santa Monica, Cal., *Roentgenology.*
436. Horrigan, Arthur J., Springfield, Mass., *Roentgenology.*
437 Howard, Campbell, New York, N. Y., *Radiology.*
438. Howard, William P., Albany, N. Y., *Roentgenology.*
439. Howes, William E., Brooklyn, N. Y., *Radiology.*
440. Hubeny, M. J., Chicago, Ill., *Roentgenology.*
441. Huber, Frank, New York, N. Y., *Roentgenology.*
442. Hufford, Clarence E., Toledo, O., *Radiology.*
443. Hunt, Howard B., Omaha, Neb., *Radiology.*
444. Hunt, Russell R., Providence, R. I., *Roentgenology.*
445. Hunter, James W., Jr., Norfolk, Va., *Radiology.*
446. Hussey, Frank L., Chicago, Ill., *Roentgenology.*
447. Hutchinson, R. W., Chelsea, Mass., *Roentgenology.*
448. Hutton, Frederick C., Philadelphia, Pa., *Roentgenology.*
449. Hyde, Allan P., Sharon, Pa., *Roentgenology.*
450. Hyde, X. R., Fort Worth, Tex., *Roentgenology.*
451. Hynes, John F., Wilmington, Del., *Therapeutic Radiology*
452. Hynes, William P., Washington, D. C., *Therapeutic Radiology.*

453. Ikeda, Kano, St. Paul, Minn., *Roentgenology.*
454. Illick, H. Earl, New York, N. Y., *Roentgenology.*
455. Imboden, Harry M., New York, N. Y., *Roentgenology.*
456. Ingber, Irving S., San Francisco, Cal., *Radiology.*
457. Irwin, W. A., Detroit, Mich., *Radiology.*
458. Ivey, H. B., Goldsboro, N. C., *Radiology.*

459. Jaches, L., New York, N. Y., *Radiology.*
460. Jackson, Byron H., Scranton, Pa., *Radiology.*
461. Jackson, John B., Kalamazoo, Mich., *Roentgenology.*
462. Jacobs, Alexander W., New York, N. Y., *Therapeutic Radiology.*
463. Jacobs, Lewis G., Jr., Madison, Wis., *Radiology.*
464. Jacox, Harold W., Pittsburgh, Pa., *Radiology.*
465. Jahn, Albert G., Passaic, N. J., *Roentgenology.*
466. Jarre, Hans A., Detroit, Mich., *Radiology.*
467. Jenkinson, David L., Chicago, Ill., *Roentgenology.*
468. Jenkinson, E. L., Chicago, Ill., *Radiology.*
469. Jewell, Earl B., Fort Dodge, Ia., *Roentgenology.*
470. Johannesson, Carl J., Walla Walla, Wash., *Roentgenology.*
471. Johns, Erwin W., Albuquerque, N. M., *Radiology.*
472. Johnson, Brantley M., Chicago, Ill., *Roentgenology.*
473. Johnson, Clayton R., Los Angeles, Cal., *Roentgenology.*
474. Johnson, Ellsworth, Winchester, Va., *Roentgenology.*
475. Johnson, Jesse B., Galveston, Tex., *Radiology.*
476. Johnson, Sydney E., Louisville, Ky., *Diagnostic Roentgenology.*
477. Johnson, Vincent C., Ann Arbor, Mich., *Radiology.*
478. Johnston, Zoe Allison, Pittsburgh, Pa., *Therapeutic Radiology.*
479. Jones, Glifford F., Cleveland, O., *Roentgenology.*
480. Jones, Horace C., Detroit, Mich., *Radiology.*
481. Jones, J. William, Pottsville, Pa., *Radiology.*
482. Jones, Oscar O., Shreveport, La., *Roentgenology.*
483. Jones, William A., Kingston, Ont., *Radiology.*
484. Judson, Herbert A., Los Angeles, Cal., *Roentgenology.*
485. Judy, William S., Greenville, S. C., *Radiology.*

486. Kabakjian, Armen E., Lancaster, Pa., *Radiology.*
487. Kahn, Max, Baltimore, Md., *Roentgenology.*
488. Kalbfleisch, William K., Wheeling, W. Va., *Roentgenology.*
489. Kann, U. S., Binghamton, N. Y., *Radiology.*
490. Kaplan, Ira I., New York, N. Y., *Therapeutic Radiology.*
491. Kaplan, Morris, New York, N. Y., *Diagnostic Roentgenology.*
492. Kapo, Peter J., Mahanoy City, Pa., *Radiology.*
493. Kasabach, Haig H., New York, N. Y., *Radiology.*
494. Kautz, Friedrich G., New York, N. Y., *Roentgenology.*
495. Kean, Albert, New York, N. Y., *Therpaeutic Radiology.*
496. Keddy, Russell A., Stamford, Conn., *Diagnostic Roentgenology.*
497. Keichline, John M., Huntingdon, Pa., *Radiology.*
498. Keith, David Y., Louisville, Ky., *Radiology.*
499. Kelley, Jacob S., Providence, R. I., *Roentgenology.*
500. Kellogg, John O., San Diego, Cal., *Radiology.*
501. Kelly, James F., Omaha, Neb., *Radiology.*
502. Kenning, John C., Detroit, Mich., *Radiology.*

503. KERBY, JAMES P., Salt Lake City, Utah, *Roentgenology*
504. KERR, H. DAHNEY, Iowa City, Ia., *Radiology.*
505. KESMODEL, KARL F., Birmingham, Ala., *Radiology.*
506. KIBBY, SYDNEY V., Los Angeles, Cal., *Diagnostic Roentgenology.*
507. KIDDER, FRANK W., Los Angeles, Cal., *Diagnostic Roentgenology.*
508. KILBY, WALTER L., Baltimore, Md., *Radiology.*
509. KING, EARL H., Saratoga Springs, N. Y., *Roentgenology.*
510. KING, J. CASH, Memphis, Tenn., *Radiology.*
511. KINNEY, KENNETH K., Willimantic, Conn., *Roentgenology*
512. KINNEY, LYELL C., San Diego, Cal., *Radiology.*
513. KINNEY, MILA A. JACKSON, Los Angeles, Cal., *Radiology.*
514. KIRKLAND, A. STANLEY, St. John, N. B., *Roentgenology.*
515. KIRKLIN, B. R., Rochester, Minn., *Radiology.*
516. KLAPPROTH, HERMAN, Halstead, Kans., *Roentgenology.*
517. KLEIN, WILLIAM, New Brunswick, N. J., *Radiology.*
518. KLOSTERMYER, L. L., Warsaw, N. Y., *Diagnostic Roentgenology.*
519. KNAPP, JOHN C., Woodhaven, L. I., N. Y., *Radiology.*
520. KNIGHT, RUSSELL W., Brantford, Ont., *Radiology.*
521. KOIRANSKY, GENNADY H., Long Island City, N. Y., *Diagnostic Roentgenology.*
522. KOLVOORD, THEODORE, Battle Crrek, Mich., *Diagnostic Roentgenology.*
523. KORNBLUM, KARL, Philadelphia, Pa., *Radiology.*
524. KRAFT, ERNEST, New York, N. Y., *Roentgenology.*
525. KUEGLE, F. H., Janesville, Wis., *Roentgenology.*
526. KUGLER, JOSEPH C., Jackson, Mich., *Roentgenology.*
527. KUHLMAN, FRED Y., Springfield, Ill., *Roentgenology.*
528. KURZ, BERNARD, Bronx, N. Y., *Diagnostic Roentgenology.*

529. LACHMANN, ERNST, Oklahoma City, Okla., *Radiology.*
530. LAFFERTY, R. H., Charlotte, N. C., *Radiology.*
531. LAMB, FRANK W., Portland, Me., *Diagnostic Roentgenology.*
532. LAMPE, ISADORE, Ann Arbor, Mich., *Radiology.*
533. LANDAU, GEORGE M., Chicago, Ill., *Roentgenology.*
534. LANDES, W. L. S., York, Pa., *Roentgenology.*
535. LANG, THEODOR, Rockford, Ill., *Radiology.*
536. LANGAN, PAUL C., Akron, O., *Diagnostic Roentgenology.*
537. LANGE, SIDNEY, Cincinnati, O., *Radiology.*
*538. LANGER, HEINZ, Pittsburgh, Pa., *Therapeutic Radiology.*
539. LANGILL, MORTON H., Worcester, Mass., *Roentgenology.*
540. LANIER, LEON M., Nashville, Tenn., *Radiology.*
541. LANMAN, EVERETT L., Battle Creek, Mich., *Roentgenology*
542. LAPE, C. PEARLEY, Buffalo, N. Y., *Diagnostic Roentgenology.*
543. LARKEY, CHARLES J., Bayonne, N. J., *Diagnostic Roentgenology.*
544. LARKIN, LEO P., Ithaca, N. Y., *Roentgenology.*
545. LARSEN, WILLIAM W., Le Mars, Ia., *Roentgenology.*
546. LATTMAN, ISIDORE, Washington, D. C., *Radiology.*
547. LAW, F. M., New York, N. Y., *Diagnostic Roentgenology.*
548. LAWRENCE, W. S., Memphis, Tenn., *Radiology.*
549. LAWSON, JOHN D., Sacramento, Cal., *Radiology.*
550. LEDDY, E. T., Rochester, Minn., *Radiology.*
551. LEDOUX, ALFRED C., Evanston, Ill., *Radiology.*
552. LEEF, EDWARD, San Francisco, Cal., *Radiology.*
553. LEFEVRE, WALTER I., Cleveland, O., *Roentgenology.*
554. LEHMAN, J. S., Philadelphia, Pa., *Radiology.*
555. LEIBERT, HARRY F. Bethlehem, Pa., *Roentgenology.*
556. LENZ, MAURICE, New York, N. Y., *Therapeutic Radiology.*
557. LEONARD, RALPH D., Boston, Mass., *Roentgenology.*
558. LEUCUTIA, T., Detroit, Mich., *Radiology.*
559. LEVENE, GEORGE, Boston, Mass., *Roentgenology.*
560. LEVI, IRWIN P., Anniston, Ala., *Roentgenology.*
561. LEVIN, ALFRED G., Miami, Fla., *Radiology.*
562. LEVIN, ISAAC, New York, N. Y., *Radiology.*
563. LE VINE, DAVID, El Dorado, Ark., *Diagnostic Roentgenology.*
564. LEVINE, SAMUEL, Philadelphia, Pa., *Radiology.*
565. LEVITIN, JOSEPH, San Francisco, Cal., *Radiology.*
566. LEVY, ABRAHAM, Brooklyn, N. Y., *Diagnostic Roentgenology.*
567. LEVYN, LESTER, Buffalo, N. Y., *Diagnostic Roentgenology*
568. LEWIS, RAYMOND W., New York, N. Y., *Diagnostic Roentgenology.*
569. LHEVINE, MORRIS B., Tulsa, Okla., *Roentgenology.*
570. LIEBMAN, CHARLES, Montreal, Que., *Roentgenology.*
571. LILJEDAHL, ELMER N., Los Angeles, Cal., *Roentgenology.*
572. LINGEMAN, LESLIE R., Rochester, N. Y., *Roentgenology.*
573. LINGLEY, JAMES R., Boston, Mass., *Radiology.*
574. LIPSCHULTZ, OSCAR, Minneapolis, Minn., *Roentgenology.*
575. LITSCHGI, JOSEPH J., Chicago, Ill., *Roentgenology.*
576. LITTIG, L. V., Madison, Wis., *Radiology.*
577. LOCHRY, RALPH L., Indianapolis, Ind., *Roentgenology.*
578. LOCKHART, REUBEN H., Bridgeport, Conn., *Radiology.*
579. LOCKWOOD, IRA H., Kansas City, Mo., *Radiology.*
580. LOUD, NORMAN W., New Britain, Conn., *Diagnostic Roentgenology.*
581. LOUGHERY, THOMAS P., Philadelphia, Pa., *Roentgenology.*
582. LOVERUD, HAROLD I. L., Manchester, N. H., *Radiology.*
583. LUBELL, MOSES F., Waterville, Me., *Roentgenology.*
584. LUCAS, CHARLES D., Charlotte, N. C., *Therapeutic Radiology.*
585. LUCINIAN, JOSEPH H., Miami, Fla., *Roentgenology.*
586. LUTZ, JEREMIAH F., York, Pa., *Roentgenology.*
587. LUTZE, FREDERICK H., Brooklyn, N. Y., *Therapeutic Radiology.*
588. LYONS, CLINTON G., Hines, Ill., *Diagnostic Roentgenology.*

589. MACCOLL, D. R., Los Angeles, Cal., *Roentgenology.*
590. MACCOMB, W. S., New York, N. Y., *Therapeutic Radiology.*
591. MACFARLAND, WILLIAM J., Hornell, N. Y., *Roentgenology.*
592. MCCARTHY, HUMPHREY L., Boston, Mass., *Roentgenology.*
593. MCCARTHY, JUSTIN E., Cincinnati, O., *Radiology.*
594. MCCAW, WILLIAM W., Washington, D. C., *Radiology.*
595. MCCLANAHAN, CHARLES W., West Los Angeles, Cal., *Radiology.*
596. MCCLELLAND, DONALD C., Lafayette, Ind., *Radiology.*
599. MCCLURE, C. C., Nashville, Tenn., *Radiology.*
*598. MCCORMICK, ARTHUR F., Du Bois, Pa., *Roentgenology.*
599. MCCORMICK, H. G., Laurel, Miss., *Roentgenology.*
600. MCCORMICK, NORMAN A., Windsor, Ont., *Therapeutic Radiology.*
601. MCCORMICK, WILLIAM M., Du Bois, Pa., *Roentgenology.*
602. MCCULLOUGH, JOHN F., Pittsburgh, Pa., *Radiology.*
603. MCDEED, WINFIELD G., Houston, Tex., *Roentgenology.*
604. MCDERMOTT, JOSEPH L., Kansas City, Mo., *Radiology.*
605. MCELFATRICK, GEORGE C., Wilmington, Del., *Roentgenology.*
606. MCEUEN, HARRY B., Jacksonville, Fla., *Radiology.*
607. MCGAUGHEY, H. D., Joplin, Mo., *Radiology.*
608. MCGEE, HARRY H., Savannah, Ga., *Roentgenology.*
609. MCGEHEE, WILLIAM H., Fresno, Cal., *Roentgenology.*
610. MCGLOTHLAN, ARTHUR B., St. Joseph, Mo., *Radiology.*
611. MCGREGOR, WILLIAM J., Wilkinsburg, Pa., *Roentgenology.*
612. MCGUFFIN, W. HERBERT, Calgary, Alberta, *Radiology.*
613. MCHENRY, RUPERT K., Houston, Tex., *Roentgenology.*
614. MCINTOSH, HARRIET C., New York, N. Y., *Roentgenology.*
615. MCKINNEY, JOSEPH T., Roanoke, Va., *Roentgenology.*
616. MCNABB, ATHOLL M., Ottawa, Ont., *Roentgenology.*
617. MCNAMEE, EDGAR P., Cleveland, O., *Roentgenology.*
618. MCNUTT, JOHN R., Duluth, Minn., *Radiology.*
619. MCPEAK, CLARENCE N., Fitchburg, Mass., *Roentgenology.*
620. MCPEAK, EDGAR M., Washington, D. C., *Radiology.*
621. MACMILLAN, A. S., Boston, Mass., *Diagnostic Roentgenology.*
622. MADDOX, WILLIAM H., Wauseon, O., *Diagnostic Roentgenology.*
623. MAGRUDER, L. FREELAND, Norfolk, Va., *Radiology.*
624. MAHRER, HERBERT A., Cleveland, O., *Roentgenology.*
625. MAIER, ROE J., Chicago, Ill., *Radiology.*
626. MALCOLMSON, PATRICK H. Edmonton, Alberta, *Radiology.*
627. MALONE, LEANDER A., Terre Haute, Ind., *Radiology.*
628. MANDEVILLE, FREDERICK B., Richmond, Va., *Radiology.*
*629. MANGES, WILLIS F., Philadelphia, Pa., *Radiology.*
630. MARCHBANKS, S. S., Chattanooga, Tenn., *Radiology.*
631. MARKS, HIRSCH, New York, N. Y., *Therapeutic Radiology.*

632. Marks, Joseph H., Fall River, Mass., *Roentgenology.*
633. Marquis, W. James, Newark, N. J., *Roentgenology*
634. Martin, Charles L., Dallas, Tex., *Radiology.*
635. Martin, Hayes E., New York, N. Y., *Therapeutic Radiology.*
636. Martin, James M., Dallas, Tex., *Radiology.*
637. Martin, Thomas W., Port Arthur, Tex., *Diagnostic Roentgenology.*
638. Martin, W. C., Louisville, Ky., *Roentgenology.*
639. Mason, Claude H., El Paso, Tex., *Diagnostic Roentgenology.*
640. Massaro, Alfonso F., New York, N. Y., *Diagnostic Roentgenology.*
641. Masterson, John J., Brooklyn, N. Y., *Roentgenology.*
641. Marlack, James A., Longmont, Colo., *Diagnostic Roentgenology.*
643. Matthews, Cora A., Evanston, Ill., *Roentgenology.*
644. Mattick, Walter L., Buffalo, N. Y., *Radiology.*
645. Mayer, William W., Jersey City, N. J., *Roentgenology.*
645. Mawhinney, Harvey N., Pittsburgh, Pa., *Diagnostic Roentgenology.*
647. May, Ernst A., East Orange, N. J., *Radiology.*
648. May, Raymond V., Cleveland, O., *Radiology.*
649. May, Robert J., Cleveland, O., *Radiology.*
650. Mayfield, Claud, Long Beach, Cal., *Diagnostic Roentgenology.*
651. Meadows, James A., Birmingham, Ala., *Radiology.*
652. Means, Hugh H., Columbus, O., *Radiology.*
653. Medelman, John P., St. Paul, Minn., *Roentgenology.*
654. Meland, Orville N., Los Angeles, Cal., *Therapeutic Radiology.*
655. Meltzer, Samuel L., Portsmouth, O., *Diagnostic Roentgenology.*
656. Mendelson, Emanuel, Brooklyn, N. Y., *Roentgenology.*
*657. Menees, Thomas O., Grand Rapids, Mich., *Radiology.*
658. Menville, Leon J., New Orleans, La., *Radiology.*
659. Merchant, Albert K., Philadelphia, Pa., *Radiology.*
660. Merrill, E. Forrest, New York, N. Y., *Roentgenology.*
661. Merritt, E. A., Washington, D. C., *Radiology.*
662. Mesirow, Sidney D., Chicago, Ill., *Roentgenology.*
663. Meter, Edward G., Reading, Pa., *Radiology.*
664. Meyer, Keith T., Evansville, Ind., *Roentgenology.*
665. Meyer, William H., New York, N. Y., *Radiology.*
666. Miles, John M., New Orleans, La., *Diagnostic Roentgenology.*
667. Milkman, Louis A., Scranton, Pa., *Radiology Roentgenology.*
668. Miller, Harry A., Baltimore, Md., *Radiology.*
669. Miller, Russel F., Philadelphia, Pa., *Radiology.*
670. Millwee, Robert H., Dallas, Tex., *Radiology.*
671. Ming, Charles M., Okmulgee, Okla., *Radiology.*
672. Minor, Edward G., Detroit, Mich., *Diagnostic Roentgenology.*
673. Moffatt, F. J., Medford, Ore., *Diagnostic Roentgenology.*
674. Moloney, Albert M., Boston, Mass., *Roentgenology.*
675. Moore, Alexander B., Washington, D. C., *Radiology.*
676. Moore, Claude, Washington, D. C., *Radiology.*
677. Moore, Daniel M., Monroe, La., *Roentgenology.*
678. Moore, John J., San Francisco, Cal., *Radiology.*
679. Moore, Paul D., Muncie, Ind., *Radiology.*
680. Moore, Sherwood, St. Louis, Mo., *Radiology.*
681. Moore, Vernor M., Grand Rapids, Mich., *Radiology.*
682. Morrison, Murray C., London, Ont., *Radiology.*
683. Morrison, Sidney L., Boston, Mass., *Roentgenology.*
684. Morse, Russell W., Minneapolis, Minn., *Roentgenology.*
685. Morton, S. A., Milwaukee, Wis., *Radiology.*
686. Moses, Chester D., Buffalo, N. Y., *Diagnostic Roentgenology.*
687. Mosteller, Malcolm, Columbia, S. C., *Radiology.*
688. Mostrom, H. T., Batavia, Ill., *Radiology.*
689. Moxness, Bennie A., Dayton, O., *Diagnostic Roentgenology.*
690. Mueller, W. K., St. Louis, Mo., *Diagnostic Roentgenology.*
691. Mulligan, Peter B., Ashland, Pa., *Roentgenology.*
692. Murphy, G. W., Asheville, N. C., *Roentgenology.*
693. Murphy, J. T., Toledo, O., *Radiology.*
694. Myers, Ralph E., Oklahoma City, Okla., *Radiology.*
695. Napper, Marvin L., Tulsa, Okla., *Roentgenology.*
696. Naslund, Ames W., St. Paul, Minn., *Roentgenology.*
697. Nathanson, Louis, Brooklyn, N. Y., *Radiology.*
698. Nelson, Peter A., Chicago, Ill., *Therapeutic Radiology.*
699. Nessa, N. J., Sioux Falls, S. D., *Roentgenology.*
700. Newcomer, Nathan B., Denver, Colo., *Radiology.*
701. Newcomet, William S., Philadelphia, Pa., *Radiology.*
702. Newell, Robert R., San Francisco, Cal., *Radiology.*
703. Nichols, B. H., Cleveland, O., *Radiology.*
704. Nichols, Harold E., Seattle, Wash., *Diagnostic Roentgenology.*
705. Noble, Robert P., Raleigh, N. C., *Roentgenology.*
706. Nordin, Gustaf T., Minneapolis, Minn., *Radiology.*
707. O'Bannon, R. P., Fort Worth, Tex., *Radiology.*
708. O'Boyle, Cyril P., Philadelphia, Pa., *Radiology.*
709. O'Brien, Frederick W., Boston, Mass., *Radiology.*
710. O'Connell, Andrew E., Worcester, Mass., *Roentgenology.*
711. O'Neill, John R., San Francisco, Cal., *Roentgenology.*
712. Ochsner, Harold C., Indianapolis, Ind., *Radiology.*
713. Oderr, Charles, Jersey City, N. J., *Roentgenology.*
714. Oechsli, Waldo R., Olive View, Cal., *Diagnostic Roentgenology.*
715. Oehlbeck, Luther W., Clifton Springs, N. Y., *Roentgenology.*
716. Ogden, Ralph T., Hartford, Conn., *Radiology.*
717. Olin, Harry, Chicago, Ill., *Roentgenology.*
718. Orndoff, B. H., Chicago, Ill., *Radiology.*
719. Orr, Clifford R., Buffalo, N. Y., *Radiology.*
720. Osgood, Herman A., Boston, Mass., *Roentgenology.*
721. Osmond, John D., Cleveland, O., *Roentgenology.*
722. Osmond, Leslie H., Pittsburgh, Pa., *Radiology.*
723. Ossip, Abraham, New York, N. Y., *Diagnostic Roentgenology.*
724. Ostro, Marcus, Baltimore, Md., *Roentgenology.*
725. Ostrum, Herman W., Philadelphia, Pa., *Roentgenology.*
726. Ourian, Adom K., New York, N. Y., *Diagnostic Roentgenology.*
727. Overgaard, Anders P., Omaha, Neb., *Radiology.*
728. Owen, Arthur K., Topeka, Kans., *Roentgenology.*
729. Owen, Colin C., San Bernardino, Cal., *Roentgenology.*
730. Pack, George T., New York, N. Y., *Therapeutic Radiology.*
*731. Paine, Robert, Memphis, Tenn., *Radiology.*
732. Pallen, Conde deS., Rochelle Park, N. J., *Therapeutic Radiology.*
733. Palmer, Dorwin L., Portland, Ore., *Radiology.*
734. Pancoast, Henry K., Philadelphia, Pa., *Radiology.*
735. Parker, Carl H., Pasadena, Cal., *Roentgenology.*
736. Parker, Eugene M., Houston, Tex., *Roentgenology.*
737. Parmelee, B. M., Bridgeport, Conn., *Radiology.*
738. Parry, Leo D., Easton, Pa., *Radiology.*
739. Paterson, Robert K., Ottawa, Ont., *Radiology.*
740. Paul, Lester W., Kansas City, Mo., *Radiology.*
741. Pawling, Jesse R., Watertown, N. Y., *Diagnostic Roentgenology.*
742. Payton, Frazier J., Miami Beach, Fla., *Radiology.*
743. Peake, John D., Mobile, Ala., *Radiology.*
744. Peck, Willis S., Ann Arbor, Mich., *Radiology.*
745. Peden, Joseph C., St. Louis, Mo., *Roentgenology.*
746. Peirce, Carleton B., Ann Arbor, Mich., *Radiology.*
747. Pendergrass, E. P., Philadelphia, Pa., *Radiology.*
748. Pendergrass, Robert C., Americus, Ga., *Roentgenology.*
749. Pepe, John, Brooklyn, N. Y., *Roentgenology.*
750. Percival, Milton F., Philadelphia, Pa., *Radiology.*
751. Perkins, Charles W., Norwalk, Conn., *Roentgenology.*
752. Perkins, Roy S., Boston, Mass., *Roentgenology.*
753. Perlberg, Harry J., Jersey City, N. J., *Roentgenology.*
754. Perley, Arthur E., Waterloo, Ia., *Radiology.*
755. Perry, Gentz, Evanston, Ill., *Radiology.*

756. PERRY, SOLOMON P., Sayre, Pa., *Radiology.*
757. PETERS, ANTHONY E., Auburn, Me., *Roentgenology.*
758. PETERS, CHESTER M., Canton, O., *Radiology.*
759. PETERS, JESSE J., Tuskegee, Ala., *Diagnostic Roentgenology.*
760. PETERSON, CHARLES H., Roanoke, Va., *Roentgenology.*
761. PETERSON, GEORGE E., Waukesha, Wis., *Radiology.*
762. PETERSON, V. L., Charleston, W. Va., *Radiology.*
763. PETRIE, E. A., St. John, N. B., *Roentgenology.*
764. PETT, ROBERT G., Pittsburgh, Pa., *Radiology.*
765. PETTIT, ROSWELL T., Ottawa, Ill., *Therapeutic Radiology.*
766. PFAHLER, G. E., Philadelphia, Pa., *Radiology.*
767. PFEFFER, THEODORE J., Racine, Wis., *Radiology.*
768. PHILIPS, HERMAN B., New York, N. Y., *Radiology.*
769. PHILLIPS, CLYDE C., Charlotte, N. C., *Radiology.*
770. PIERCE, HAROLD J., Terre Haute, Ind., *Radiology.*
771. PIERSON, JOHN W., Baltimore, Md., *Radiology.*
772. PIGOTT, ALBERT W., Skillman, N. J., *Diagnostic Roentgenology.*
773. PINDELL, MERL L., Los Angeles, Cal., *Diagnostic Roentgenology.*
774. PINES, JOHN A., Orlando, Fla., *Therapeutic Roentgenology.*
775. PIRIE, A. H., Montreal, Que., *Radiology.*
776. PITMAN, JAMES F., Lake City, Fla., *Roentgenology.*
777. PITTS, THOMAS A., Columbia, S. C., *Roentgenology.*
778. PLEHN, GEORGE J., New York, N. Y., *Diagnostic Roentgenology.*
*779. PODLASKY, HARRY B., Milwaukee, Wis., *Roentgenology.*
780. POHLE, E. A., Madison, Wis., *Therapeutic Radiology.*
781. POMERANZ, MAURICE M., New York, N. Y., *Radiology.*
782. POMERANZ, RAPHAEL, Newark, N. J., *Roentgenology.*
783. POMEROY, LAWRENCE A., Cleveland, O., *Radium Therapy.*
784. POOL, HARRY H., Pontiac, Mich., *Roentgenology.*
785. POPOFF, CONSTANTINE, Haverhill, Mass., *Diagnostic Roentgenology.*
786. POPP, WALTER C., Rochester, Minn., *Therapeutic Radiology.*
787. POPPEL, MAXWELL H., New York, N. Y., *Diagnostic Roentgenology.*
788. PORTER, HORACE W., Jackson, Mich., *Radiology.*
789. PORTMANN, U. V., Cleveland, O., *Radiology.*
790. POST, JOSEPH W., Philadelphia, Pa., *Diagnostic Roentgenology.*
791. POTTER, CARLTON F., Syracuse, N. Y., *Roentgenology.*
792. POTTER, HOLLIS E., Chicago, Ill., *Roentgenology.*
793. POTTER, ROY P., Marshfield, Wis., *Roentgenology.*
794. POUND, ROBERT E., New York, N. Y., *Roentgenology.*
795. POWELL, E. V., Temple, Tex., *Radiology.*
796. POWERS, MARTIN T., Utica, N. Y., *Diagnostic Roentgenology.*
797. POWERS, RICHARD T., Springfield, Mass., *Radiology.*
798. POWERS, ROBERT A., Palo Alto, Cal., *Radiology.*
799. PRESENT, ARTHUR J., New York, N. Y., *Radiology.*
800. PRICE, R. J., Dayton, O., *Radiology.*
801. PROUTY, J. V., Terre Haute, Ind., *Radiology.*
802. PUTTS, B. SWAYNE, Erie, Pa., *Roentgenology.*
803. QUICK, DOUGLAS, New York, N. Y., *Therapeutic Radiology.*
804. QUIGLEY, D. T., Omaha, Neb., *Radium Therapy.*
805. QUIMBY, A. JUDSON, New York, N. Y., *Roentgenology.*
*806. QUINEY, JAMES J., Easton, Pa., *Radiology.*
807. QUINLAN, CATHERINE M., Santa Rosa, Cal., *Roentgenology.*
808. RAAP, GERARD, Miami, Fla., *Radiology.*
809. RADDING, MOSES B., Elizabeth, N. J., *Radiology.*
810. RATHBONE, RALPH R., Washington, D. C., *Radiology.*
811. RAUSCHENBACH, CHARLES W., Hammond, Ind., *Roentgenology.*
812. RAVOLD, HENRY J., St. Joseph, Mo., *Radiology.*
813. RAY, WILLIAM B. G., Pittsburgh, Pa., *Roentgenology.*
814. REAVES, HUGH G., Knoxville, Tenn., *Roentgenology.*
815. REED, CHARLES B., Newburgh, N. Y., *Roentgenology.*
816. REES, SHERMAN E., Portland, Ore., *Radiology.*
817. REEVES, ROBERT J., Durham, N. C., *Radiology.*
818. REILEY, WILLIAM E., Clearfield, Pa., *Radiology.*
819. REINEKE, HAROLD G., Cincinnati, O., *Roentgenology.*
820. REITTER, GEORGE S., East Orange, N. J., *Radiology.*
821. REMER, JOHN, New York, N. Y., *Therapeutic Roentgenology.*
822. RENDICH, RICHARD A., Brooklyn, N. Y., *Roentgenology.*
823. REYNOLDS, GARDNER S., Walker, Minn, *Diagnostic Roentgenology.*
824. REYNOLDS, LAWRENCE, Detroit, Mich., *Radiology.*
825. RHINEHART, DARMON A., Little Rock, Ark., *Roentgenology.*
826. RHUDY, BOOKER E., Greensboro, N. C., *Roentgenology.*
827. RICE, FRANK M., San Francisco, Cal., *Roentgenology.*
828. RICHARDS, CHARLES M., San Jose, Cal., *Radiology.*
829. RICHMAN, SAMUEL, New York, N. Y., *Radiology.*
830. RICHMAN, SAMUEL H., Chicago, Ill., *Diagnostic Roentgenology.*
831. RIEBEL, FRANK A., Columbus, O., *Radiology.*
832. RIGLER, LEO G., Minneapolis, Minn., *Radiology.*
833. RITVO, MAX, Boston, Mass., *Radiology.*
834. RITZMAN, ALLEN Z., Harrisburg, Pa., *Roentgenology.*
835. ROBERTS, DOUGLAS J., Hartford, Conn., *Radiology.*
836. ROBERTS, JOSEPH E., JR., Camden, N. J., *Radiology.*
837. ROBIN, NATHANIEL H., Hempstead, N. Y., *Roentgenology.*
838. ROBIN, PERCIVAL A., Hempstead, N. Y., *Roentgenology.*
839. ROBINS, SAMUEL A., Boston, Mass., *Roentgenology.*
840. ROBINSON, G. ALLEN, New York, N. Y., *Therapeutic Radiology.*
*841. ROBINSON, RALPH V., Pittsburgh, Pa., *Roentgenology.*
842. ROBINSON, WALTER W., Memphis, Tenn., *Roentgenology.*
843. RODENBAUGH, F. H., San Francisco, Cal., *Radiology.*
844. RODGERS, FLOYD D., Columbia, S. C., *Radiology.*
845. RODICK, J. C., New Orleans, La., *Roentgenology.*
846. RODRIGUEZ, JUAN, Fort Wayne, Ind., *Radiology.*
847. ROEMER, JACOB, Paterson, N. J., *Radiology.*
*848. ROLAND, MARION M., Oklahoma City, Okla., *Therapeutic Radiology.*
849. RONA, MAURICE, New Brunswick, N. J., *Roentgenology.*
850. RORK, LEE W., Hastings, Neb., *Roentgenology.*
851. ROSE, CASSIE B., Boulder, Colo., *Radiology.*
852. ROSENBAUM, GEORGE, Philadelphia, Pa., *Diagnostic Roentgenology.*
853. ROSH, RIEVA, New York, N. Y., *Therapeutic Radiology.*
854. ROTHNEM, THOMAS P., Fargo, N. D., *Roentgenology.*
855. ROUSSEAU, J. P., Winston Salem, N. C., *Radiology.*
856. ROWE, EDWARD W., Lincoln, Neb., *Radiology.*
857. ROWELL, EDWARD E., Stamford, Conn., *Roentgenology.*
858. RUBENFELD, SIDNEY, New York, N. Y., *Therapeutic Radiology.*
859. RUBERT, SAMUEL R., Chicago, Ill., *Roentgenology.*
860. RUDE, JOE C., New York, N. Y., *Radiology.*
861. RUDISILL, HILLYER, JR., Charleston, S. C., *Radiology.*
862. RUGGLES, HOWARD E., San Francisco, Cal., *Roentgenology.*
863. RULISON, FOSTER C., Syracuse, N. Y., *Roentgenology.*
864. RUTLEDGE, CLIFFORD P., Shreveport, La., *Radiology.*
865. RYAN, ERIC J., New York, N. Y., *Roentgenology.*
866. RYPINS, EDWIN L., Bloomington, Ill., *Radiology.*
867. SAMUEL, ERNEST C., New Orelans, La., *Roentgenology.*
868. SANDERSON, STEVENS S., Detroit, Mich., *Radiology.*
869. SANTE, L. R., St. Louis, Mo., *Radiology.*
870. SARGENT, WILLIAM H., Oakland, Cal., *Radiology.*
871. SCHATZKI, RICHARD, Boston, Mass., *Radiology.*
872. SCHECHTER, SAMUEL, New York, N. Y., *Diagnostic Roentgenology.*
873. SCHENCK, SAMUEL G., Brooklyn, N. Y., *Radiology.*
874. SCHIMMELPFENNIG, R. D., Montclair, N. J., *Roentgenology*
875. SCHMIDT, ERNST A., Denver, Colo., *Radiology.*
876. SCHMITZ, HENRY, Chicago, Ill., *Therapeutic Radiology.*
877. SCHMITZ, WALTER A., Middletown, N. Y., *Roentgenology.*
878. SCHNACK, A. G., Honolulu, Hawaii, *Radiology.*
879. SCHNOEBELEN, PAUL C., St. Louis, Mo., *Roentgenology.*
880. SCHONS, EDWARD, St., Paul, Minn., *Radiology.*
881. SCHREINER, BERNARD F., Buffalo, N. Y., *Therapeutic Radiology.*
882. SCHUMACHER, F. L., Pittsburgh, Pa., *Radiology.*
883. SCHWARTZ, CHARLES W., New York, N. Y., *Roentgenology.*

884. Schwartz, Irving, New York, N. Y., *Diagnostic Roentgenology.*
885. Scott, Clifton R., New Haven, Conn., *Roentgenology.*
886. Scott, Walter R., Niagara Falls, N. Y., *Roentgenology.*
887. Scott, Wendell G., St. Louis, Mo., *Radiology.*
888. Scott, Wilhelmina S., Lancaster, Pa., *Radiology.*
889. Seeds, Asa E., Spokane, Wash., *Radiology.*
890. Sender, Arthur C., Philadelphia, Pa., *Roentgenology.*
891. Seward, William H., Orange, N. J., *Radiology.*
892. Shapiro, Abraham V., Brooklyn, N. Y., *Diagnostic Roentgenology.*
893. Shapiro, William M., Toledo, O., *Radiology.*
894. Sharpe, A. Maxwell, Chester, Pa., *Roentgenology.*
895. Shaw, W. McL., Jacksonville, Fla., *Roentgenology.*
896. Shebesta, Emil M., Detroit, Mich., *Radiology.*
897. Sheldon, Francis B., Stockton, Cal., *Radiology.*
898. Sheridan, William M., Spartanburg, S. C., *Radiology.*
*899. Sherman, Herbert deG., White Plains, N. Y., *Diagnostic Roentgenology.*
900. Sherrick, Earl C., Connellsville, Pa., *Diagnostic Roentgenology.*
901. Shetter, North W., Lakewood, O., *Roentgenology.*
902. Shiflett, E. Lee, Louisville, Ky., *Roentgenology.*
903. Shoemaker, Robert 3rd, Philadelphia, Pa., *Radiology.*
904. Shohan, Joseph, Greensboro, N. C., *Roentgenology.*
905. Shore, O. J., Detroit, Mich., *Diagnostic Roentgenology.*
906. Shoulders, H. S., Nashville, Tenn., *Radiology.*
907. Shull, J. Rush, Charlotte, N. C., *Roentgenology.*
908. Shulman, Simon, Far Rockaway, N. Y., *Roentgenology.*
909. Sichler, Harper G., Lafayette, Ind., *Radiology.*
910. Sickels, Thomas N., Watertown, N. Y., *Roentgenology.*
911. Siefert, Alfred C., Oakland, Cal., *Radiology.*
912. Sigman, Frederick G., Salisbury, N. C., *Roentgenology.*
913. Sims, George P., Columbus, O., *Therapeutic Radiology.*
914. Sinberg, Samuel E., New York, N. Y., *Diagnostic Roentgenology.*
915. Singleton, Arthur C., Toronto, Ont., *Radiology.*
916. Skinner, Edward H., Kansas City, Mo., *Radiology.*
917. Skomp, C. E., Denver, Colo., *Diagnostic Roentgenology.*
918. Smedal, M. I., Boston, Mass., *Radiology.*
919. Smith, Arthur B., La Jolla, Cal., *Diagnostic Roentgenology.*
920. Smith, B. B., Buffalo, N. Y., *Diagnostic Roentgenology.*
921. Smith, Jerome H., San Angelo, Tex., *Radiology.*
922. Smith, Lester A., Indianapolis, Ind., *Radiology.*
923. Smith, Richard L., Santa Monica, Cal., *Radiology.*
924. Smith, R. Manges, Philadelphia, Pa., *Roentgenology.*
925. Smith, Roscoe L., Lincoln, Neb., *Radiology.*
926. Smyth, Thomas L., Allentown, Pa., *Roentgenology.*
927. Snead, Lawrence O., Richmond, Va., *Roentgenology.*
928. Snedden, Alexander R., McKeesport, Pa., *Diagnostic Roentgenology.*
929. Snoke, Paul O., Lancaster, Pa., *Radiology.*
930. Snow, Henry, Dayton, O., *Radiology.*
931. Snow, William, New York, N. Y., *Roentgenology.*
932. Snure, Henry, Los Angeles, Cal., *Roentgenology.*
933. Soiland, Albert, Los Angeles, Cal., *Radiology.*
934. Solis-Cohen, Leon, Philadelphia, Pa., *Radiology.*
935. Sosman, M. C., Boston, Mass., *Radiology.*
936. Soule, Arthur B., Jr., Burlington, Vt., *Roentgenology.*
937. Spackman, Edgar W., Philadelphia, Pa., *Radiology.*
938. Spangler, Davis, Dallas, Tex., *Radiology.*
939. Spencer, Hunter B., Lynchburg, Va., *Roentgenology.*
940. Spencer, Jack, Boston, Mass., *Radiology.*
941. Spies, John W., Bombay, India, *Therapeutic Radiology.*
942. Spillman, Ramsay, New York, N. Y., *Diagnostic Roentgenology.*
943. Spilman, Harold A., Ottumwa, Ia., *Roentgenology.*
944. Spinzig, Egdar W., St. Louis, Mo., *Radiology.*
945. Sproull, John, Haverhill, Mass., *Roentgenology.*
946. Squire, Fay H., Chicago, Ill., *Roentgenology.*
947. Stafford, Owen R., Los Angeles, Cal., *Therapeutic Roentgenology.*
948. Stall, Arthur H., Akron, O., *Radiology.*
949. Stammel, Charles A., Fort Benning, Ga., *Diagnostic Roentgenology.*
950. Starks, Dorothy J., Palo Alto, Cal., *Radiology.*
951. Startz, Irving S., Elmhurst, N. Y., *Roentgenology.*
952. Stayton, Chester A., Indianapolis, Ind., *Radiology.*
953. Stecher, William R., Darby, Pa., *Radiology.*
954. Steel, David, Cleveland, O., *Roentgenology.*
955. Stein, Justin J., Hines, Ill., *Therapeutic Radiology.*
956. Steinberg, Samuel S., Butte, Mont., *Radiology.*
957. Steiner, Joseph M., New York, N. Y., *Roentgenology.*
958. Stenstrom, Annette T., Minneapolis, Minn., *Diagnostic Roentgenology.*
959. Stephenson, F. B., Denver, Colo., *Radiology.*
960. Stevens, R. H., Detroit, Mich., *Radiology.*
961. Stewart, Harry M., Johnstown, Pa., *Radiology.*
962. Stewart, Melba D., Laconia, N. H., *Roentgenology.*
963. Stewart, Ralph C., Lowell, Mass., *Roentgenology.*
964. Stewart, Wendell, East St. Louis, Ill., *Diagnostic Roentgenology.*
965. Stewart, William H., New York, N. Y., *Roentgenology.*
966. Stiles, Henry T., Cleveland, O., *Roentgenology.*
967. Stocking, Bruce W., New York, N. Y., *Radiology.*
968. Stone, Robert S., San Francisco, Cal., *Roentgenology.*
969. Stowe, Irving E., Portsmouth, N. H., *Diagnostic Roentgenology.*
970. Strauss, Abraham, Cleveland, O., *Radium Therapy.*
971. Strauss, Hyman, Brooklyn, N. Y., *Radium Therapy.*
972. Stuart, Leon H., Tulsa, Okla., *Roentgenology.*
973. Sussman, Marcy L., New York, N. Y., *Radiology.*
974. Sutherland, Charles G., Rochester, Minn., *Diagnostic Roentgenology.*
975. Swearingen, Forrest C., Pomona, Cal., *Radiology.*
976. Swenson, Paul C., New York, N. Y., *Roentgenology.*
977. Swope, Opie W., Wichita, Kans. *Radiology.*
978. Sycamore, Leslie K., Hanover, N. H., *Radiology.*
979. Tabb, John L., Jr., Richmond, Va., *Roentgenology.*
980. Taft, Robert B., Charleston, S. C., *Radiology.*
981. Talley, Daniel D., Jr., Richmond, Va., *Roentgenology.*
982. Tamarkin, Saul J., Youngstown, O., *Radiology.*
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989. Templeton, Frederic E., Chicago, Ill., *Radiology.*
990. Tennis, Matthew N., Fall River, Mass., *Roentgenology.*
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1002. Troje, Oscar R., Fairfield, Ala., *Radiology.*
1003. Trostler, Isador S., Chicago, Ill., *Radiology.*
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1016. VAN ALLEN, HARVEY W., Springfield, Mass., *Radiology.*
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1098. YOUNG, JAMES L. R., New York, N. Y., *Therapeutic Radiology.*
1099. ZEITLIN, NATHAN S., Chicago, Ill., *Roentgenology.*
1100. ZILIAK, A. LAWRENCE, Bay City, Mich., *Roentgenology.*
1101. ZIMMERMAN, CARL A. W., Cape Girardeau, Mo., *Diagnostic Roentgenology.*
1102. ZINK, OSCAR C., St. Louis, Mo., *Radiology.*
1103. ZULICK, J. DONALD, Philadelphia, Pa., *Roentgenology.*

* Deceased.

The Board will hold two examinations during 1938, the first at the Mark Hopkins Hotel in San Francisco, June 10–12, and the second at the time and place of the meeting of one of the two national radiologic societies, depending on which society meets at the more convenient place. Those wishing to appear for examination in San Francisco should have their applications on file by March 1.

For Information communicate with the Secretary, 102–110 Second Avenue S. W., Rochester, Minnesota.

B. R. KIRKLIN, M.D.
Secretary-Treasurer

AMERICAN BOARD OF RADIOLOGY

At the annual meeting of the American Board of Radiology, held in Atlantic City, June, 1937, the following requirements and recommendations as to professional training were adopted:

The purpose of this report is to outline the method or methods which are recommended for graduate training in radiology. The specific requirements to which the Board of Radiology is committed at present are:

A. Professional Education*
   1) Graduation from a medical school of the United States or Canada, recognized by the Council on Medical Education and Hospitals of the American Medical Association.
   2) Completion of an interneship of not less than one year in a hospital approved by the same Council.
   3) Three years' training in Radiology or sufficient experience in lieu thereof.

B. Special Training* (To be effective January 1, 1940)
   1) A period of study after the interneship of not less than three years in an institution or radiological department recognized by the same Council and the Board of Radiology as competent to provide a satisfactory training in the field of Radiology, or equivalent training acceptable to the Board.
   2) This period of specialized preparation shall include:
      a) Graduate training in pathologic anatomy, radiophysics and radiobiology;
      b) An active experience of not less than twenty-four months in a radiological department recognized by the Board and the Council as capable of providing satisfactory training;
      c) Examination in the basic sciences of radiology as well as in the clinical aspects thereof.

In the final analysis the most important element in adequate radiologic training is not the school, nor the content or arrangement of the course, but the instructor. He should be endowed with the ability not only to teach, but also to inspire, to stimulate and to impart by example those principles and that attitude of mind conducive to the best practice of radiology. Similarly, the future of radiology depends not on the type or formula of the course nor on the accuracy or thoroughness of the instruction, but on the qualification of the candidate for training, and careful selection of candidates is the very foundation of successful education, for an excellent course cannot make a proficient radiologist out of poor material but an apt student may acquire competence despite limitations of opportunity. With this factor in mind, the Board suggests that the proper approach to graduate training in radiology is through a hospital or institutional residency and that the candidate be selected or approved by the radiologist in charge.

There is universal agreement among teachers of radiology with the general principles outlined above, but there is considerable divergence of opinion as to the best manner of executing them, the order in which subjects should be taken up and the time that should be allotted to the various subdivisions of radiology. Such differences are not only inevitable but also desirable, for radiologic education is still in the developmental stage, and its progress would be hampered by too rigid standardization at this time. Institutions vary as to the character of material at their command, and hence instructors differ in opinion as to the emphasis that should be laid on particular subjects. Because of these differences a precise and detailed plan of instruction that would be appropriate at one institution might be largely inapplicable at another. Thus the American Board of Radiology feels that it is wise to allow generous latitude in the course of training it prescribes and that at present it is inadvisable to list and narrowly define all the subjects that might well be taught or assign definite periods of study for each of them.

Accordingly, the specifications enumerated are broad and flexible, and it will be left to the future to determine what course

* In case of an applicant whose training has been received outside of the United States and Canada, the credentials must be satisfactory to the Advisory Board for Medical Specialties.

or combination of courses will produce the best qualified radiologists. Among exceptions to this generalization, however, the Board wishes to stress the importance of pathology as a fundamental science in radiology. Roentgen examination, diagnostic interpretation and treatment rest primarily on concepts of pathologic processes. For this reason the Board feels that at least six months of the first year should be devoted to the study of pathology and pathologic anatomy with particular emphasis on gross pathology and that of tumors. Much of the required work in other basic sciences can be carried out along with the clinical, and no set period of time or other specification need be established at present; for example, physics can be reviewed during the study of radiotherapy. In general, the Board is of the opinion that the first year should be given to pathology and roentgen technique and toward acquiring the broad radiologic viewpoint, and that the second and third years should be given to the clinical applications of radiology, with at least six months devoted entirely to radiotherapy. Theses, advanced degrees and original research are outside the province of present requirements.

B. R. KIRKLIN, M.D.
Secretary-Treasurer

To the Editor:

If Dr. A. Vaughn Winchell* will consult the *Archives of Radiology and Electrotherapy* for July, 1917, he will find that I was the original compounder of the formula of an indelible ink for the skin. Subsequent experience has shown that it is necessary to keep the ink well stoppered and to renew it when it has become oxidized at all, because its value lies in its soaking into the skin in an unoxidized form, when it is brown, and its subsequent oxidization causes it to stain the horny layer black. It is also found that the addition of a small quantity of sulphurous acid will retard the tendency to oxidization in the bottle. It remains much longer on some skins than on others.

N. S. FINZI

London, England

* Winchell, A. V., An indelible ink for the skin. AM. J. ROENTGENOL. & RAD. THERAPY, Nov., 1937, *38*, 790.

GEORGIA RADIOLOGICAL SOCIETY

The Georgia Radiological Society was organized at the Palmer House, Chicago, during the Fifth International Congress of Radiology. The first regular meeting was held in Atlanta, Georgia, on November 27, at the Academy of Medicine. The program consisted of a round table discussion of difficult diagnostic cases and of therapy problems. Fifteen radiologists were present. A constitution and by-laws were adopted and plans made for the next meeting in conjunction with the Medical Association of Georgia at Augusta, Georgia, in the spring of 1938. The meeting was followed by a luncheon at the Biltmore. The officers of the Society are: President, James J. Clark, Atlanta; Vice-President, William F. Lake, Atlanta; Secretary-Treasurer, Robert C. Pendergrass, Americus.

EASTERN RADIOLOGISTS

The Program Committee has selected the Warwick Hotel, 1701 Locust Street, Philadelphia, as the headquarters for the coming Conference of Eastern Radiologists which meets on January 28 and 29, 1938. All of the scientific presentations will be held at the Hotel. The scientific sessions are to be held Friday morning and afternoon and Saturday morning, while Saturday afternoon has been reserved for those who wish to visit the various roentgen-ray departments and laboratories of the Philadelphia group.

MIDWESTERN RADIOLOGISTS

The second annual Clinical Conference of Midwestern Radiologists will be held in Kansas City, Missouri, February 11 and 12, 1938, with headquarters at the Muehlebach Hotel.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as a space permits.

Elements of Nuclear Physics. By Franco Rasetti, Professor of Spectroscopy, Royal University of Rome, Research Associate, Columbia University. Cloth. Price, $4.50. Pp. 327, with 73 illustrations. New York: Prentice-Hall, Inc., 1936.

The book is characterized by unusual clarity of style, and by its logical presentation of the essential known facts of nuclear physics. By careful selection and arrangement of the material, the author has been able to embody much more in this book than the term "elements" implies.

The first four chapters deal with the fundamental phenomena of natural radioactivity, from experimental and theoretical standpoints, and incorporate the extension of the subject to interactions of emissions whose energies exceed those obtainable from naturally radioactive substances. Chapter V deals with the known properties of atomic nuclei, and with modern nuclear theory, founded on quantum mechanics and on recent experiments on nuclear transformation.

With this necessary background, the author describes the various types of artificial disintegration produced by various disintegrating agents, the stable or radioactive products formed, and gives many illustrations of the nuclear reactions and energies involved. A final chapter is devoted to the salient features of cosmic radiation.

The 73 figures include 8 plates of cloud chamber photographs, mass spectrograms, β-ray spectrograms, etc., which illustrate some of the means by which important nuclear phenomena are observed and measured. The 37 tables provide convenient and accurate reference material on natural radioactivity, isotopic constitution of the elements, nuclear reactions, and a table of most of the well-substantiated artificially radioactive elements, the nuclear transformations by which they are produced, their decay constants, and the kinds and energies of their radiations.

This book should be read by anyone interested in any phase of nuclear physics or in any application of naturally or artificially radioactive material, neutrons, or hard γ-radiation. As an introduction to this new and ever-widening field, and as a source-book for a variety of useful information, it will have lasting value.

Gordon L. Locher

Diagnosis and Treatment of Malignant Tumors. Stanford University School of Medicine, September, 1937.

This 82 page paper bound syllabus in electrotype was prepared for students enrolled in the postgraduate course dealing with neoplasms offered by Stanford University. The material was prepared jointly by members of the staff engaged in teaching this course and represents an unusually complete and comprehensive survey of the subject. Roughly, the first third of the volume is devoted to introductory remarks concerning the cancer problem in general and to a terse straightforward presentation of the principles of radiation therapy. The remainder of the book deals specifically with the major clinical forms of malignant neoplasm, following in each case a comparable plan of arrangement. There are many well chosen references under each section.

The reader is frequently pleasantly surprised with the direct frankness and brevity of style. The chapter on radiation therapy is particularly well done, and though it is confined to ten pages, no essential consideration has been omitted or neglected. The book is distinctly a syllabus and not a textbook and yet it is just the sort of ready reference for which there is such definite need in familiarizing students and practitioners of medicine with well-established facts and accepted principles of tumor treatment. In every way this is a thoroughly commendable contribution.

F. J. Hodges

Roetgenganzaufnahmen des Menschen: Darstellung des normalen Skeletts seiner ererbten und erworbenen Veränderungen. Von Dr. Robert Janker, Privatdozent an der Universität Bonn. Mit einem Geleitwort von Prof. Dr. E. von Redwitz, Bonn. Cloth. Pp. 17, with 40 plates Leipzig: Johan Ambrosius Barth, 1934.

Recently some orthopedists have found it advantageous to study the entire spine or the entire lower extremity by means of a film of extra size. The study of the entire body by a single roentgenogram has been chiefly limited to use in exhibits. Dr. Janker has produced a very interesting volume in his study of human beings by "total roentgenograms." His method permits of the study of the skeleton and soft tissues, as a whole, and gives a clearer conception of the general nature of certain diseases and the interrelation of changes observed in various parts of the body.

His forty full body roentgenograms show the various normal types of individuals including the leptosome, pycnic, muscular, and mixed types. They also show some twenty pathological, conditions including dwarfism, myxedema, acromegaly, chondrodystrophy, osteogenesis imperfecta, generalized exostoses, periostitis hyperplastica.

The author has overcome many technical difficulties in producing these interesting studies. To overcome loss of detail and distortion he has used a distance of 4.5 meters and a supine position by placing his tube on the ceiling. With so great a distance, the factors of tube capacity, small focal spot and exposure time were made difficult but he has met these problems very successfully. Uniformity of penetration and contrast are also well taken care of in most of the views, thanks to the painstaking and laborious technique.

This is pioneer work and no doubt by studying his methods improvements will be made. As for the subject matter, the author states that he has by no means exhausted the field of usefulness of this type of study.

To make the book more valuable to those who do not read German well, the entire contents including text, titles and index are translated in parallel columns into English.

The book must be seen to have the striking effect of the skeleton as a whole appreciated. It deserves a place in all medical libraries and should be of special interest to anatomists, endocrinologists, and orthopedists, as well as to roentgenologists.

E. Walter Hall

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NECK AND CHEST

JORESS, MARK H. Primary tuberculosis. *Am. Rev. Tuberc.*, Jan., 1936, *33*, 55–60.

The author reviews some of the pathological, clinical, and roentgenological phases of the subject and describes several cases to illustrate the points in question.

According to the writer, the diagnosis of primary tuberculosis is based upon the development of pulmonary lesions of marked chronicity which, in the majority of patients, can only be demonstrated roentgenographically. The lack of clinical signs and symptoms serves to distinguish it from the adult or reinfection type of tuberculosis, generally accompanied by toxemia and lung destruction.

In spite of its brevity, the article contains a wealth of material.—*P. J. Hodes.*

AMBERSON, J. BURNS, JR. The process of resolution in pulmonary tuberculosis. *Am. Rev. Tuberc.*, March, 1936, *33*, 269–301.

Resolution, as a rule, begins in the zone of collateral inflammation and gradually spreads toward the center of the pneumonic lesion. Since little or no sputum is produced during resolution, one must infer that the exudate is absorbed. In infants, pneumonic lesions resolve strikingly. Similar lesions in adults and negroes usually ulcerate. One must remember that the involved lung is never restored to its normal state.

Microscopic study of lung tissue taken from patients well ten to eighteen years following resolution revealed interstitial fibrosis, emphysema, distortion of the pulmonary bronchioles, and varices in the lung tissue. This latter finding may explain hemoptysis sometimes encountered in clinically healed cases. The emphysema may account for the lack of roentgen visualization of small infiltrations due to relative increases in air content.

The author has included several case histories and excellent illustrations which are of considerable value.—*P. J. Hodes.*

REISNER, DAVID. Pulmonary tuberculosis of the lower lobe. *Arch. Int. Med.*, August, 1935, *56*, 258–280.

Primary tuberculosis of the lower lobe is observed in the ratio of about 18 women to 1 man. There seems to be no tendency for this type of tuberculosis to occur more commonly in colored people. The average age in the group of patients studied by this author was twenty-nine years.

Clinically, these cases are unusual, because the first symptoms suggest a grippe-like or pneumonia-like syndrome. Over 50 per cent of the patients with lower lobe tuberculosis can date the onset of symptoms back for a period between two to eight weeks. From the roentgen standpoint, one is impressed by the frequency with which tuberculosis of the lower lobe involves the right side. One is further impressed by the frequency with which cavities are found in patients examined for the first time. This is interesting, as it suggests a tendency to more easy ulceration and cavity formation. This suggestion is substantiated by the fact that the cavities found in the apex of the lower lobe are usually much larger than one would expect from the history alone. Bronchiogenic spread into the other portions of the lower lobe is fairly characteristic. It has been noticed, however, that these acinar or sublobular foci are more diffuse than those seen in association with bronchiogenic dissemination from upper lobe tuberculosis. While caudal dissemination is the rule, lower lobe tuberculosis may spread into the base and even the apex of the upper lobe.

The author discusses the prognosis and treatment of this condition. The roentgen illustrations of lower lobe tuberculosis included in this article enhance its value.—*P. J. Hodes.*

MCPHEDRAN, F. MAURICE. The distribution and prognosis of pulmonary lesions; associated tuberculous and non-tuberculous. *Am. J. M. Sc.*, Nov., 1935, *190*, 659–672.

This report is based upon a comprehensive review of the roentgen and clinical findings in 51 patients with sputum-positive lesions who became sputum-negative, with little or no treatment. The author believes that extensive nontuberculous lesions in the paracardiac portions of the lower lobes influence apical tuberculosis beneficially. He has frequently seen apical lesions regress rapidly and even heal

under the influence of nonspecific infections in these paracardiac zones. This relationship seems even more significant when one realizes that the author has seen apical infections grow larger as the basal infections showed evidence of clearing only to regress again later as the basal infections flare up.

This interesting concept, of mutually opposed activity, is critically analyzed by the author who presents considerable evidence which seems to support his theory. The article is well illustrated.—*P. J. Hodes.*

Maxwell, James. Lung abscess. *Lancet*, Aug. 22, 1936, *2*, 413–416.

Lung abscess is a nontuberculous suppuration with cavitation occurring in the lung tissue. The conditions most frequently giving rise to pulmonary suppuration are mouth operations, pneumonia, foreign body, bronchial carcinoma, and septic upper abdominal conditions.

The causation of lung abscess is still a moot subject. According to some, the majority of lung abscesses result from aspiration of infected material; others believe they are embolic in origin. Both theories are tenable but both are probably dependent upon some condition in the lung originally which makes it susceptible to invasion.

The author reviews the clinical findings calling attention to the fact that abundant foul sputum is not always present. The sequelae and diagnostic procedures are also discussed.

Treatment in most cases should be passive. Bed rest is of great importance and may be all that is necessary. Organic arsenical compounds intravenously may do much to promote healing. Bronchoscopy should be resorted to after other methods have failed. Artificial pneumothorax, of questionable value, should never be used when lesions lie close to the pleura. Such lesions are best treated surgically.—*P. J. Hodes.*

Pollock, William C. Pulmonary cystic disease. *Am. Rev. Tuberc.*, Oct., 1936, *34*, 527–539.

The author recognizes no single etiological factor in the production of lung cysts. A study of 3 patients suggested that the cysts resulted from developmental defects in the bronchial tree. While the defect may be congenital, its development may take years.

The three case histories have one clinical finding in common, progressive dyspnea. All were apparently well until adult life. The roentgenograms revealed huge radiolucent areas easily confused with pneumothorax. The author discusses the rôle of bronchoscopy, bronchography, thoracentesis and pneumothorax in the identification of these lesions.—*P. J. Hodes.*

Steidl, John, and Heise, Fred H. Bilateral apical nontuberculous bronchiectasis. *Am. Rev. Tuberc.*, Jan., 1936, *33*, 61–65.

The author presents the clinical and laboratory finding in a patient thought to have bilateral apical bronchiectasis. Excellent reproductions of the patient's chest films aid considerably in following the arguments presented substantiating the diagnosis rather than tuberculosis or cystic disease.—*P. J. Hodes.*

Mayer, Edgar, and Grethmann, Wolfgang. Silicosis; some differential diagnostic problems. *Am. Rev. Tuberc.*, March, 1936, *33*, 313–321.

This is a brief review of certain interesting problems of silicosis. The author stresses the importance of the history of exposure and roentgenograms in the diagnosis of silicosis. The relationship between physical characteristics of dust particles and rate of development of pulmonary changes is mentioned.

Three essential types of abnormal roentgen findings in silicosis are described and an attempt made to classify the various types of involvement. Several case histories are presented to illustrate points in question.—*P. J. Hodes.*

Middleton, E. L. Industrial pulmonary disease due to the inhalation of dust. *Lancet*, July 4, 1936, *2*, 1–9.

After a brief, though comprehensive, survey of the clinical, pathological, and roentgen findings in silicosis, the author reviews the silica hazard in various industries. In doing this, special attention is given to the material and the kind of dust to which workers are exposed during their employment.

In discussing the sand blasting hazard, the author states that the short period of employment and rapid course of the disease are features found in various parts of the world. Flint and pebble crushing were less dangerous in

spite of extremely high dust counts. The manufacture of abrasive soaps, which entails handling a 98 per cent silica quartzite, is very dangerous. The occupational histories and ultimate developments in a group of patients working in this industry are tabulated. Metal grinding, tunnel mining, slate, gold, tin and iron ore mining hazards are also included. It is interesting to note that a grave digger, working in sandstone, developed tuberculosilicosis after seventeen years of exposure. The author also analyzes the coal mining and pottery industries.

This is an excellent article for reference.—*P. J. Hodes.*

MIDDLETON, E. L. Industrial pulmonary disease due to the inhalation of dust. *Lancet*, July 11, 1936, *2*, 59–64.

Clinically, asbestosis presents few signs in its early stages. As the disease progresses dyspnea gradually becomes evident. A fine type of fibrosis occupying the lower portions of both lungs is usually seen roentgenographically. The ground glass appearance of the lungs and shaggy cardiac contour are also described. The author lists the various processes in the asbestos industry and their respective particle counts. Anatomical descriptions of the pulmonary and pleural fibrosis and descriptions of "asbestosis bodies" complete the brief review.

Sillimonite, anhydrous aluminum silicate, is used as a refractory material. The material is of interest because its fibrous form resembles asbestos. A small group of individuals exposed to this dust presented no evidences of pneumoconiosis. China clay, a hydrated aluminum silicate, talc, and French chalk, are also innocuous though roentgenographic changes suggesting minimal fibrosis have been described. Since sericite is frequently found in association with quartz it has been considered by some as hazardous. The evidence at present available is insufficient to allow a definite statement regarding sericite and pulmonary fibrosis. While certain pulmonary changes have been produced by silicates, the roentgen and pathological signs set it apart from typical silicosis.

This is an excellent article for reference.—*P. J. Hodes.*

EGBERT, DAN S., and GEIGER, ARTHUR J. Pulmonary asbestosis and carcinoma. *Am. Rev. Tuberc.*, July, 1936, *34*, 143–150.

The clinical and anatomical findings are presented in a case of pulmonary asbestosis with an associated primary carcinoma of the lung. The patient was employed as a weaver in an asbestos factory for eighteen years. At necropsy both pleural cavities were completely obliterated by firm fibrous adhesions. Asbestos bodies were scattered throughout both lungs. While the association between pulmonary asbestosis and carcinoma is unique, the author speculates upon their interrelationship on the basis of chronic irritation.—*P. J. Hodes.*

SOKOLOFF, MARTIN J. Anthracosilicosis and tuberculosis. *Am. Rev. Tuberc.*, Nov., 1936, *34*, 700–711.

This report from a sanatorium in Pennsylvania concerns itself with the problem of tuberculosis in silicotics. While data published about 1910 suggested that tuberculosis was not a great hazard in coal miners, the present statistics reveal that it occurred in 56 per cent of 418 anthracite miners. The explanation offered incriminates the "jackhammer" as the old hand drill did not create as fine a dust.

The authors call attention to the distinctive character of the lesions of tuberculosis in silicosis. The wide distribution of the caseous nodules and lack of the usual apical infiltration are usual.

The various examinations of assistance in establishing the presence of tuberculosis in a miner are discussed and the toxic and non-toxic clinical pictures described.—*P. J. Hodes.*

ZAVOD, WILLIAM A. Fibrin bodies in the pleural space in a case of artificial pneumothorax. *Am. Rev. Tuberc.*, Jan., 1936, *33*, 48–54.

The author describes the findings in a patient with fibrin bodies in the pleural space, of whom a complete study was made.

The diagnosis is not difficult, most fibrin bodies being demonstrated roentgenographically as sharply outlined dense shadows, frequently movable with change of position. Grossly, fibrin bodies are usually flat or oval with ivory-colored smooth and glistening surfaces.

Their mode of origin is still controversial. Most men believe that fibrin bodies are formed either by agglomeration of fibrin in a pleural effusion or as the result of hemorrhage into the pleural space.—*P. J. Hodes.*

CARMAN, H. FRANK. Bilateral artificial pneumothorax in the treatment of pulmonary tuberculosis. *Am. Rev. Tuberc.*, April, 1936, *33*, 491–501.

This is an excellent synopsis of the present status of bilateral pneumothorax in tuberculosis. The indications and contraindications for bilateral pneumothorax are clearly defined. The author stresses the dangers associated with the procedure. The importance of thorough familiarity with the physiology of the cardio-respiratory system cannot be overestimated. Several case records and excellent chest reproductions add considerable interest to the article.—*P. J. Hodes.*

Glickman, L. Grant, and Schlomovitz, Benjamin H. Simultaneous bilateral spontaneous pneumothorax complicating pneumonoconiosis. *Am. Rev. Tuberc.*, Sept., 1936, *34*, 390–401.

The author presents the findings and roentgenograms of a rare case of spontaneous bilateral pneumothorax in a silicotic. A review of the literature revealed few authenticated cases.

The patient, a hard-coal miner, was found to have second stage pneumoconiosis. He was followed roentgenographically for one year during which he developed bilateral collapse.

At post-mortem examination large emphysematous bullae and tuberculous cavities were found which might have precipitated pneumothorax. Both lungs were infiltrated by a dense fibrosis with relatively recent tuberculosis.—*P. J. Hodes.*

Corsello, Joseph N., and Bruckheimer, Ralph M. Bilateral simultaneous artificial pneumothorax in the treatment of pulmonary tuberculosis. *Am. Rev. Tuberc.*, April, 1936, *33*, 502–521.

The authors report results of bilateral simultaneous artificial pneumothorax in 36 patients with advanced bilateral pulmonary tuberculosis. Twenty-one of these patients have remained alive at least 1½ years and 18 of this group are clinically well. This record seems to negate the contention that this type of treatment should only be used in patients with lesions limited to both upper lobes. While the authors do not advocate indiscriminate use of bilateral pneumothorax, they do present a plea for its use in many apparently hopeless patients.

The end-results depend upon: (1) effectiveness of the collapse, (2) proper selection of cases, (3) frequency of serious complications, (4) proper cooperation between patient and doctor, and (5) the skill and diligence exercised in the treatment.

It is of interest to note that the treatment produced no noteworthy untoward happenings other than effusion into the pleural space.—*P. J. Hodes.*

Stafford, Frank B. The indications for terminating artificial pneumothorax. *Am. Rev. Tuberc.*, Sept., 1936, *34*, 402–420.

The author attempts to evaluate the various points which should be considered before terminating pneumothorax. The subject is dealt with under two headings: (1) undesirable re-expansion of the lung, and (2) voluntary re-expansion of the lung.

Undesirable re-expansion occurs following insufficient air injection, formation of adhesions, uncontrollable hydrothorax, reactivation of an old process in the contralateral lung, etc.

Voluntary re-expansion is allowed in cases of long-standing collapse in whom all symptoms are gone, sputum is negative, and the lung appears to be healthy. Considerable reliance is placed upon blood sedimentation and leukocytic reaction.

Usually fairly light infiltrations should remain collapsed for two to three years, heavy consolidations with or without thin-walled cavities at least four years, and dense fibrocaseous lesions with thick walled cavities five, six or more years.

Several case histories and good reproductions of roentgenograms are included.—*P. J. Hodes.*

Salkin, David, Cadden, A. V., and McIndoe, R. B. The blocked pulmonary cavity; an anatomical, roentgenological and clinical study. *Am. Rev. Tuberc.*, 1936, *34*, 634–648.

The authors demonstrate that cavities may exist in the lung without any communication with the tracheobronchial tree. In order to do this, a mixture of potassium iodide, barium, and milk was instilled into lungs after death by means of tracheal cannulas and thoracentesis needles, and the results followed roentgenographically and anatomically.

Non-communications were found in 26 per cent of the 70 tuberculous patients studied. Of a total of 147 cavities (over 3 cm. in diameter), 14 per cent did not communicate with bronchi. The causes of non-communication were found to be intracavitary, extrabronchial and intrabronchial. Intracavitary blocks were due to

material within the cavity. Extrabronchial blocks consisted of fibrosis and cicatrization incorporating the air channel and cavity. Intrabronchial obstructions were due to obstructing plugs and tuberculous bronchitis. Kinking was rarely encountered.

The study refutes the beliefs that (1) blocking a bronchus causes healing of a cavity, and (2) failure of filling a cavity with lipiodol means that no cavity exists. The prognosis of blocked cavities does not differ from closed ones.—*P. J. Hodes.*

SALKIN, DAVID, CADDEN, A. V., and MCINDOE, R. B. Post-mortem bronchography. *Am. Rev. Tuberc.*, Nov., 1936, *34*, 649–662.

This is an extremely interesting and important communication. Post-mortem bronchography has allowed the authors to study the dynamics of bronchi and alveoli in relatively healthy lungs and in tuberculosis. They found no difference in the distribution of the bronchial tree and the secondary lobules before and after death.

The authors found that when alveolar filling was absent the alveoli had been destroyed, collapsed, filled with pus, exudate, or blood, or the bronchi obstructed. Bronchial blocks were common and were due to secretion, blood or pus. Blocking of a major bronchus occurred in 12 patients and was not associated with atelectasis. It was of considerable interest to find other evidence substantiating the theory of interlobar air channels in patients with bronchiectasis.

The authors are convinced that radiopaque solutions can penetrate any part of the lung that air can enter. They do not believe that delayed alveolar filling is due to air absorption but consider it a function of the viscosity of the injected material and its ability to displace alveolar air.

Pneumothorax produced alveolar collapse but pneumoperitoneum proved of no value in its production.—*P. J. Hodes.*

JOANNIDES, MINAS. Acute primary diaphragmitis (Hedblom's syndrome). *Am. J. M. Sc.*, April, 1935, *189*, 566–570.

Acute primary diaphragmitis, preferably called Hedblom's syndrome, is characterized by painful breathing, painful cough, costal breathing, and fixation of the diaphragm. The primary type usually follows an acute upper respiratory infection, whereas secondary invasion may be associated with infections above and below the diaphragm. Hedblom's syndrome is frequently associated with upper abdominal pain. This pain has been attributed to the intimate relationship existing between the transversus abdominus and the diaphragm.

Pathologically, the diaphragm shows changes of an acute exudative and proliferative inflammation. Sometimes, scar tissue replaces the muscle fibers producing a change in the normal roentgen appearance of the dome of the diaphragm.—*P. J. Hodes.*

ABDOMEN

ROSS, J. COSBIE. The use of lipiodol in surgery of the biliary passages. *Lancet*, Feb. 1, 1936, *1*, 251–254.

Evidence has accumulated indicating that missed biliary calculi account for approximately 4 per cent of second abdominal operations. Under the best conditions, with the assistance of bougie, catheters, and irrigations, it is possible to miss a small stone, especially when the ampulla is thickened and chronic pancreatitis is present. Lipiodol injection will not only indicate whether a block is partial or complete, but it will also demonstrate the site of the obstruction and exclude spasm. If lipiodol is held up in the common duct or its supraduodenal portion it usually indicates stricture. Ampullary blockage is commonly due to stone if one can exclude spasm. In the latter case, a second roentgen examination taken three-quarters of an hour after injection of atrophine may reveal that the lipiodol has passed into the duodenum. If, on the other hand, the lipiodol is persistently held up at the ampulla, a stone is very probable.

The author enumerates the possible dangers of the method and presents several case histories to illustrate points in question.—*P. J. Hodes.*

ROENTGEN AND RADIUM THERAPY

MELCHART, FRANZ, and SCHLOSS, WILHELM. Die Radium-Röntgen Simultantherapie des Mammakarzinoms. (Simultaneous radium-roentgen treatment of cancer of the breast. *Strahlentherapie*, 1935, *52*, 20–30.

The authors describe a method of treatment of cancer of the breast in which roentgen and radium irradiation are used simultaneously. The method must not be used in cases with

any serious affection of the lungs, no matter whether it is carcinomatous or not.

The first step in the treatment is to introduce the radium needles under local anesthesia. The number of the needles and their length varies with the size of the tumor. As a rule, they yield a millicurie-destroyed for each centimeter of length in 100 hours (133 mg-hr.). They are implanted in several layers, running parallel to each other so there will be no crossing of the irradiation. The needles are covered with a sterile dressing.

A half hour later the roentgen treatment is begun. In ulcerated cases with a great deal of secretion this is preceded by electrocoagulation. In the beginning the radium doses used were small. The needles were left in the tissues 100 hours, giving about 1 millicurie-destroyed per cubic centimeter of tissue. But having found that the breast tissue bears radium irradiation very well the radium dosage was increased by protracting the time. As the roentgen treatment lasts longer than the radium this protraction not only gives a higher dosage but lengthens the period during which the two kinds of radiation act simultaneously.

In the roentgen treatment a large field was at first used covering the breast, the supraclavicular region and the axillary region; skin-focus distance 50 cm., 179 kv., filter 0.5 mm. copper and 1 mm. aluminum, 8–17 r/min.; daily dose 200–250 r with a total dose of 3,000 to 4,000 r. As the erythema was not uniformly distributed they now use three fields; the breast field is given a total dose of 2,500–3,000 r with a tube 20/20 cm.; the supraclavicular field 1,500–2,000 r with a tube 10/15 and the axilla 1,000–1,500 r with the same kind of tube. Two fields are irradiated a day with a total irradiation time of thirty to sixty minutes.

Brief histories are given of 30 cases treated in this way. Among these, 11 patients are alive and free of symptoms. The observation time has not yet reached the five-year limit so definite judgment cannot be passed on the cases. But the results illustrate the possibilities of the technique. Its further development should lie in the direction of protraction of the effective simultaneous period and decrease of the r/min. dose. Possibly the roentgen dose and the area of radium puncture can be increased.

The advantages of the method are that the two forms of radiant energy act at the same time and the skin is spared by the radium puncture.—*Audrey G. Morgan.*

Taylor, Grantley W. Carcinoma of the breast in young women. *New England J. M.*, Dec. 31, 1936, *215*, 1276–1278.

A comparative study of carcinoma of the breast as occurring in 146 individuals under forty-five years of age and in 303 cases in the age period forty-six to sixty years shows that 44 per cent of the younger individuals had highly malignant tumors in comparison with 28 per cent of such tumors in the older group. In comparable groups, as regards degree of malignancy and extent of axillary involvement, the five year cure rate was 71 per cent in the older group; 67 per cent in the younger. In cases with axillary involvement one year after operation, 95 per cent of the older women survive, as compared with 75 per cent of the younger women. There is no reason to feel that postoperative irradiation of the ovaries would have modified appreciably the results observed in the younger group.—*W. R. Brooksher.*

Lynham, J. E. A. Carcinoma of the breast. *Brit. J. Radiol.*, Jan., 1937, *10*, 60–64.

The three methods of irradiation in breast cancer, external application of radium, interstitial application of radium and roentgen rays, are fully discussed. The author feels that roentgen rays generated at 200 kv. are sufficient. Postoperative irradiation by the fractionated method is considered preferable and it is thought that the best results follow localized excision of the lesion rather than the radical removal.—*W. R. Brooksher.*

Watson, William L. Cancer of the esophagus. *New York State J. M.*, Nov., 1, 1936, *36*, 1615–1617.

Report is made of 157 cases of cancer of the esophagus, the treatment of which has been carried out along four different lines. The first group was treated by protracted irradiation with roentgen rays, the average daily exposure being 300 r with a total for each of four portals, two anterior and two posterior, with the following factors: 200 kv., 30 ma., 70 cm., 0.5 mm. Cu filter. The second group was treated by gastrostomy and the intra-esophageal application of radium element in a specially constructed tandem applicator of 30 mg. radium element strength. The total dose objective was 4,320 mg-hr. In those cases which presented complete esophageal obstruction, the third

group, gastrostomy was first performed, supplemented by heavy external irradiation, followed by divided doses with the radium tandem applicator. In the fourth group, cases theoretically operable, but which were found inoperable in all 4 cases explored, radon seeds were inserted into the lesion and adjacent structures at the time of operation. Of 68 cases treated by divided roentgen doses, 33 are alive, 8 for one year and 2 for two years.—*W. R. Brooksher.*

GIBERT, P., and SOLOMON, L. Die Röntgentherapie beim Krebs des Gebärmutterkörpers und den postmenopausischen Metrorrhagien. (Roentgen therapy in cancer of the body of the uterus and metrorrhagias after the menopause.) *Strahlentherapie*, 1935, *52*, 31–36.

There is general agreement in regard to the value of roentgen therapy in cancer of the cervix but a very marked disagreement in regard to its value in cancer of the body of the uterus. German and Scandinavian authors report very high percentages of cures—Seitz and Wintz 67 per cent cures in operable cases, Döderlein 62 per cent and the Radiumhemmet of Stockholm 66 per cent. On the contrary, French authors report very low percentages of cures—Lacassagne 16 per cent of 30 cases and the authors no cures in cases that were definitely proved by histological examination to be malignant. They treated 55 cases of post-menopause hemorrhage and brought about cessation of hemorrhage in 10 cases but in these there was no histological demonstration of malignancy.

He believes the differences in the figures are not due to different methods of treatment. They themselves used various techniques and very penetrating rays but the results were the same. The apparent differences are due to the fact that the authors who report high percentages of cures have not made a definite histological diagnosis of malignancy. Only about 60 per cent of the cases of hemorrhage after the menopause are caused by cancer; the other 40 per cent are due to benign hyperplasias of the mucous membrane or submucous myomata. These can be cured readily by roentgen treatment.

They recommend, therefore, that before operation for cancer of the body of the uterus histological examination be made of a biopsy specimen. In case of doubt as to the malignant nature of the disease, the therapeutic test should be made. That is, what he calls a provisional irradiation should be given. The patient is given a dosage of 5,000 r in four or five weeks. This dose is distributed over two fields, one on the pubis and the other on the sacrum. If within a month after this treatment is finished the bleeding has not stopped completely it is almost certain that the disease is malignant.

They do not believe that true cancer of the body of the uterus can be cured with roentgen treatment alone, at least not with any technique available at present.—*Audrey G. Morgan.*

WINTZ, HERMANN. Die erfolgreiche Strahlentherapie des Adenocarcinoma corporis. (Successful radiotherapy of adenocarcinoma of the body of the uterus.) *Strahlentherapie*, 1935, *52*, 37–50.

The author discusses Gibert and Solomon's report on their treatment of 55 cases of hemorrhage after the menopause in which they had cure only in the 10 cases that were not proved to be malignant. None of the malignant cases were saved. Gibert and Solomon conclude that the authors who have reported high percentages of cures in cancer of the body of the uterus based their conclusions on inaccurate diagnoses and that cancer of the body of the uterus cannot be cured by irradiation.

Wintz takes exception to this statement as he himself has reported more than 60 per cent cures in such cases. So have Döderlein and the Radiumhemmet. So far as his own work is concerned, he can say that his diagnoses were made histologically and he is convinced that those of the other authors were also. Among his cases are 16 who have survived the treatment more than ten years and are still free of symptoms, 2 after ten years, 3 after eleven years, 2 after twelve years, 3 after fourteen years, 3 after fifteen years, 1 after sixteen years and 2 after seventeen years. He gives brief descriptions of these 16 cases and reproduces photomicrographs showing the histological findings on which the diagnoses were based.

He then discusses the probable reasons for what he thinks are Gibert and Solomon's mistaken conclusions. It is true that it is very hard to cure advanced cases of adenocarcinoma of the uterus with irradiation. These adenocarcinomas are much less radiosensitive than the pavement epitheliomas of the cervix. They

require 125 per cent of a skin erythema dose whereas pavement cell epitheliomata require only 110 per cent. This high dosage is dangerously near that which injures the intestine so it has to be given with extreme care. Fractional dosage gives the cancer cells time to recover and therefore makes it extremely difficult to irradiate effectively without injury. He says that Gibert and Solomon's technique is not described in sufficient detail to judge accurately of just how much was given but he is inclined to think that they gave an insufficient depth dosage with too great irritation of the skin—in short that their failure to obtain results was due to defective technique. It is difficult but not impossible to cure adenocarcinoma of the uterus by irradiation.—*Audrey G. Morgan.*

Dapsy, Andreas. Über die Röntgenbehandlung der entzündlichen Erkrankungen der Uterusadnexe. (Roentgen treatment of inflammatory diseases of the adnexa.) *Strahlentherapie*, 1935, *52*, 85–96.

The author gives details of the results of roentgen treatment in 40 cases of inflammation of the adnexa of the uterus. A table summarizing the results shows cure in 4 cases, or 10 per cent, improvement in 11, or 28 per cent, unchanged 23, or 57 per cent, and suppuration in 2, or 5 per cent.

It is by no means certain that the clinical improvement was due to the irradiation, not entirely so at least. Fever declines as a result of rest in bed and improved general condition from the changed conditions of life. Similar improvement has been seen with all kinds of conservative treatment and even on rest in bed without any treatment.

Even with the small doses used—the total dose was never over 34 per cent of a skin erythema dose—there is a certain amount of danger. Wagner reports 2 cases of death from peritonitis caused by suppuration. And there is always the danger of castration or injury of the ovum. In view of these facts, the author recommends roentgen treatment of inflammations of the adnexa only in cases in which other conservative treatment has failed and there is some contraindication to operation or in cases in which it seems desirable to hasten the suppuration of the exudate and its evacuation.—*Audrey G. Morgan.*

Bowing, H. H., and Fricke, Robert E. Technic of radium treatment of carcinoma of the rectum. *Radiology*, 1937, 28, 521–526.

While recognizing that surgery is the procedure of choice in rectal cancer, radiologists are many times called upon to treat this condition because the general condition of the patient, the grade of malignancy or extent of the local disease precludes surgery. The authors advise biopsy as an aid in outlining the treatment plan. Colostomy is advisable but not always necessary, providing obstructive symptoms are not presented. Treatment plans depend upon whether a cure is to be attempted or whether palliation is the object.

The methods to procure a cure include interstitial radon irradiation, contact radiation and electrosurgery. For palliation, external irradiation with high voltage roentgen rays, radium blocks and central irradiation with radium capsules were used.—*J. H. Harris.*

Baumann-Schenker, Rudolf. Das Hamangio-Endotheliom und seine Strahlensensibilitat. (Hemangio-endothelioma and its sensitiveness to irradiation.) *Strahlentherapie*, 1935, *52*, 11–19.

Hemangio-endothelioma is a malignant tumor originating from the capillaries; it is derived partly but not wholly from the endothelium. This form of tumor is quite rare; it occurs chiefly in the thyroid, liver and bones. The author has never seen any cases in the liver but describes 4 cases in the thyroid. He works in Schinz' clinic at Zurich and goiter is very frequent in Switzerland.

The first patient was a woman, aged fifty-nine, who had an enormous tumor of the thyroid. Photographs are given showing the rapid retrogression of the tumor under roentgen treatment. A large skull metastasis developed over the right parietal and occipital bones but this too disappeared completely on roentgen irradiation. Two and a half years later she was still free of symptoms. The second patient was a woman of thirty-five. A small goiter suddenly appeared on the right side of her neck on Jan. 2, 1932, Just a year later it enlarged greatly from a sudden effusion of blood into the tumor. On Feb. 20, 1933, the tumor was removed and a diagnosis of sarcomatous struma made from histological examination. A part of the tumor was so fixed that it was impossible to remove it and protracted fractional irradiation was begun. A dosage of 5,040 r/1 was given on the

right and of 4,080 r/1 on the left, a total of 9,120 r/1. The circumference of the neck rapidly decreased. The treatment was given over a period of twenty-nine days, ending on April 4, 1933. The patient died on May 28, 1933.

The third patient was a woman of sixty-one. She had had a "thick neck" for many years but it had not caused her any trouble until recently when it enlarged suddenly and she began to have dyspnea. Protracted fractional irradiation was begun with two very small doses on account of the dyspnea. A total of 6,900 r/1 was given. Treatment was completed on Nov. 5, 1932; the patient was in good condition, the dyspnea had disappeared and the circumference of the neck had greatly decreased. The patient died on Feb. 12, 1933, from massive hemorrhage into the tumor.

Case 4 was in a man of sixty-nine; he had a large tumor of the left lobe of the thyroid. A photograph is given showing the rapid retrogression of this tumor under roentgen treatment. He is well and free of symptoms five months after a protracted fractional irradiation with a total dosage of 6,020 r/1.

All these cases show the great sensitiveness of hemangio-endothelioma to irradiation. A fifth case is described of a hemangio-endothelioma in the middle ear; it does not permit of judgment as to radiosensitiveness as the greater part of the tumor was removed surgically. Irradiation was given afterward with a total dose of 4,120 r/1 but the process extended to the base of the skull. The author does not attribute this to lack of radiosensitiveness but to the unfavorable location of the tumor.

These tumors may disappear so rapidly on roentgen treatment that it suggests a diagnosis of lymphosarcoma. In Case 1 this diagnosis would have been made if it had not been for the histological picture. But this tumor differed from lymphosarcoma even clinically in the fact that there were no metastases in distant lymph node regions.

Because of the great sensitiveness of these tumors irradiation can very well be combined with surgical treatment.—*Audrey G. Morgan.*

MEYERDING, HENRY W. Treatment of benign giant-cell tumors. *J. Bone & Joint Surg.*, Jan., 1936, *18*, 823–841.

Meyerding states that the treatment of benign giant cell tumors varies, but the physician in charge has at his disposal the means of establishing an accurate diagnosis, following which a choice of methods is determined by the condition of the patient, the site of the tumor and its size, the degree of joint disability, and damage, fracture, and the perforation or non-perforation and penetration of periosseous tissues.

He prefers to use the terms "benign giant cell tumors" and "malignant giant cell sarcomata," and in his paper he confines his discussion to the first group. He quotes previous writers who have reported metastasis of giant cell tumors in defense of this classification. To the practical surgeon this differentiation is important as delay is dangerous. Since he cannot differentiate at all times the benign and the malignant forms, he obtains consent for the type of operation which in his judgment is indicated as the best way of eradicating the tumor.

Primary irradiation of tumors based on the clinical and roentgenological findings alone is more likely to lead to error than when microscopic examination by an experienced pathologist is made. Meyerding does not believe in routine irradiation of all bone tumors, nor does he consider it advisable as a primary or sole method of treating the giant cell group of tumors. He feels that radiation treatment takes too long and causes loss of valuable time in which metastasis may occur, and that the patient may lose the opportunity of cure by more radical measures. With irradiation, both soft and osseous tissues may be damaged, radiodermatitis and ulceration may occur, and should operation be indicated, the tissue may break down, resulting in interference with conservative surgery. However, at times, irradiation is the only treatment possible and he has seen large inoperable tumors of the pelvis slowly regress and ultimately be apparently cured under its influence; for this type and for vertebral tumors and also following operation, he feels that irradiation can be recommended.

The following methods of treatment are discussed: biopsy and irradiation; curettage; curettage and irradiation; curettage and bone graft; curettage, bone graft and irradiation; resection; amputation, and reports of illustrative cases of each type of treatment.

He concludes that surgery had demonstrated its ability to cope with the majority of giant cell tumors, and, in the hands of the experi-

enced, has proved its value in bringing about a high percentage of cures. Roentgen therapy has a definite place in the treatment, and in the future, the author believes, will be found of increasing value. In his report of 61 cases, the lack of surgical complications, the duration of life after operation (3.3 years), and the high percentage of satisfactory results would indicate that cooperation between the clinician, the roentgenologist, the pathologist and the surgeon makes possible the accurate diagnosis and cure of most benign giant cell tumors of bone.—*R. S. Bromer.*

MISCELLANEOUS

Regen, Eugene M., and Wilkins, Walter E. The effect of large doses of x-rays on the growth of young bone. *J. Bone & Joint Surg.*, Jan., 1936, *18*, 61–68.

In this study 8 of a group of 14 pure-bred young rabbits of the same age were treated over the left forelegs with 2,600 r; the remaining 6 animals were used as controls. Roentgenograms of both forelegs of each animal were made at monthly intervals until growth in the controls had ceased. Growth in the radii and ulnae was followed by careful measurement of the roentgenograms for a period of eight months, giving a total of 369 observations. Sometime within the first month, growth in the treated bones stopped completely and did not reappear during the period of observation. Growth in the untreated bones of the experimental animals was not affected.

The authors believe their findings show quite definitely that bone growth, as judged by length, can be completely stopped by exposure to a sufficient dose of roentgen rays and that up to maturity of the skeleton no reappearance of growth occurs.—*R. S. Bromer.*

Regen, Eugene M., and Wilkins, Walter E. The influence of roentgen irradiation on the rate of healing of fractures and the phosphatase activity of the callus of adult bone. *J. Bone & Joint Surg.*, Jan., 1936, *18*, 69–79.

The purpose of this study was, first, to determine the effect of roentgen irradiation on the healing of fractures in adult bone by following the appearance of the fractures in the roentgenograms made at regular intervals; second, to follow the course of the phosphatase activity of these bones at the site of fracture throughout the period of healing.

The authors conclude that moderate doses of roentgen rays given previous to the production of fracture in the adult rabbit result in marked delay of union and inhibition of the rise in phosphatase activity that normally accompanies the healing of a fracture.

The possible clinical application of the findings reported in this paper and also of those reported in the paper on the effect of large doses of roentgen rays on the growth of young bones is now being investigated and the results of this study will be given in a subsequent report.—*R. S. Bromer.*

Momigliano, Emanuele. Über den Einfluss der Schilddrüsenbestrahlung auf das Ovar. (The effect of irradiation of the thyroid gland upon ovarian function.) *Strahlentherapie*, 1937, *58*, 53–73.

The normal thyroid gland is fairly radioresistant, and is one of the least radiosensitive of the endocrine glands. An excessively high total dosage is necessary to produce even slight histopathologically demonstrable changes in structure; thus, in dogs, using the physical factors as follows: 180 kv. (peak), 0.7 Zn, 26 cm. skin-target distance, 5×7 cm. fields; a total of 3 s.e.d., an s.e.d. being equivalent to 750 r, was required to produce cystic degeneration of the parenchyma, with increased interfollicular fibrosis, after an interim of four months. Identical changes are producible in humans, but the irradiation is not as well tolerated, and accordingly a rare occurrence.

Altered function of the thyroid gland produced by irradiation causes an attendant effect upon the ovaries, as shown histologically, in follicular atrophy, obliterative atresia, with concomitant hypertrophy and hyperplasia of interstitial tissue, strongly simulating cystic involution. The same appearance is found when direct irradiation of the ovaries in inducing an artificial menopause is employed. There is a direct relation between the degree of radiation effect upon the thyroid and the distant ovarian reaction. This was noted experimentally that in four months after 3 s.e.d. were applied to the thyroid effects in the ovaries approaching castration were perceived.

A factor to be considered in the radiation therapy of the thyroid in humans is the temporary glandular hyperfunction established, with incident increased radiosensitiveness, so that doses under 50 per cent s.e.d. can produce

definite results. Indubitably if the human could tolerate relatively as large doses as animals then identical results would accure as found in the author's experiments, namely, cystic degeneration.

Clinically, the confusing findings of oligomenorrhea, and amenorrhea, in the diametrically opposite entities of hyper- and hypothyroidism do occur; and, paradoxically, irradiation might be beneficial in both types. This can be explained on the assumption that the stimulating effect of irradiation on the one hand, and inhibiting influence with the gland in a state of hyperplasia and accordingly relative radiosensitivity. Of course, various remote factors of altered endocrine secretion might well enter into this complex melange; and especially the great influence of the pituitary gland. The effect of thyroidectomy and thyroid irradiation is not similar, which is explicable on the basis of varying ovarian reaction attendant on the rapid withdrawal of influencing humoral substance of the thyroid in the former, as compared to the slow compensible diminution in the latter. The result being, in thyroidectomy, a very slight ovarian alteration in both function and structure; whereas, in massive thyroid irradiation, marked involutionary ovarian changes ensue, in most instances.—*W. R. Stecher.*

INOUYE, KAZUO. Über die Beeinflussung der Röntgenstrahlenwirkung auf maligne Tumoren durch Zucker—und Insulininjektion. (The influence of sugar and insulin injection on roentgen therapy of malignant tumors.) *Strahlentherapie*, 1937, *58*, 125–142.

The author concludes after much animal experimentation that sugar injection increases the metabolism of sarcoma in canines, for there is definite increase in sugar consumption after tumor implantation; whereas the administration of insulin decreases the metabolism of the dogs in general. Clinical signs of increased local metabolism of the sarcoma, namely local heat and redness, are increased decidedly after sugar injection, and numerous cases present evidence of tumor necrosis, which is an indication of very rapid growth.

Sugar administration preceding roentgen irradiation increases the effects of the therapy on the altered metabolism of the sarcoma, making it more radiosensitive. Insulin injections after irradiation enhances the restraining action of the radiation. It is therefore advisable to give insulin after irradiation to lengthen the duration of time wherein the tumor metabolism has been altered and reduced by the effects of irradiation.

Sugar administered before the institution of roentgen therapy and then followed by irradiation aids in macroscopically diminishing the size of the tumor, and definitely increasing the life span of the animal. If the sugar is given alone, the general condition of the animal is bettered, but the growth of the sarcoma is hastened, and rapid death of the animal ensues. Irradiation alone diminishes the size of the tumor, but is somewhat harmful to the general wellbeing of the patient, and shortens the duration of life. With early irradiation, one can indubitably check the growth of implanted sarcoma in canines.—*W. R. Stecher.*

AIRD, ROBERT B. Experimental encephalography with anesthetic gases. *Arch. Surg.*, Feb., 1936, *32*, 193–217.

Because of the irritative effects of air when used to fill the ventricles, the author conducted a series of experiments to investigate the possibility of substituting some other gas which would not produce unpleasant after-effects. Dogs were the experimental animal used. A series of anesthetic gases were tried and compared with air as a medium for outlining the ventricular system in these animals. The author's conclusions are as follows:

1. A satisfactory method has been developed for testing and comparing the effect in dogs of various gases used in encephalography.

2. Injections of air, for control observations, have given results in dogs comparable in all respects to the results obtained clinically in human beings.

3. Ethyl chloride, di-vinyl chloride, ether, vinyl chloride, and acetylene proved unsatisfactory for encephalographic use, the first three being decidedly dangerous.

4. In limited series the effects of oxygen and those of cyclopropane appeared to be comparable to each other and definitely superior to those of air.

5. Because of their safety, good roentgenographic results, minimum irritation, definite sedative effect and lack of ill effects either clinically or pathologically, nitrous oxide and ethylene seem ideal agents for encephalography.—*R. P. Barden.*

Lewin, Hans. Ein neues Betrachtungsverfahren sur Verbesserung der Bildwirkung von Röntgenaufnahmen. (A new method of looking at roentgenograms to improve the effect.) *Acta radiol.*, 1936, *17*, 551–558.

The author reports a new method of viewing transparent photographs (roentgen films). The roentgenograms are inspected on a fluorescent foil instead of being looked through in the usual way. This procedure increases the contrast effect to such an extent that the density of dark areas in the film is doubled. The advantages of this technique are discussed in detail. A practical apparatus for viewing the films is described.—*Author's Abstract.*

Engelbreth-Holm, J. Über den Einfluss der Röntgenbestrahlung auf den Blutzucker bei Kaninchen und über deren Verwendbarkeit zu Blutzuckerversuchen. (The effect of roentgen irradiation on blood sugar in rabbits and their usefulness for blood sugar experiments.) *Strahlentherapie*, 1935, *52*, 101–114.

Experiments on rabbits are described in which blood sugar was tested before and after irradiation with roentgen rays. Tables are given showing the details of the results.

The increase of blood sugar after general irradiation of the whole body reported by other authors was not considered to be an immediate result of the roentgen irradiation. The results of the author's experiments indicate that it is nonspecific and only a manifestation of the great lability of blood sugar in rabbits.

The decrease of blood sugar reported by other authors after irradiation of rabbits that had been treated with gynergen could not be reproduced by the use of 1 mg. gynergen per kilogram of weight followed by irradiation with 125 r and even 500 r.

It was therefore impossible to solve the problem for which the experiments were performed, that is, to determine whether roentgen irradiation stimulates the vegetative nerve terminals in the skin. The only conclusion that can be drawn from these experiments is that if there is such an effect it is not manifested by variations in blood sugar.

Rabbits are not well adapted for experiments in which variations in blood sugar are to serve as an indicator because the blood sugar content in rabbits is not constant even under normal conditions and it reacts to many external influences with incalculable variations.—*Audrey G. Morgan.*

Gericke, W., and Leunig, H. Sterilisation von Radium- und Mesothoriumnadeln zu chirurgischen Zwecken. (Sterilization of radium and mesothorium needles for surgical purposes.) *Strahlentherapie*, 1935, *52*, 162–166.

Experiments in sterilizing radium and mesothorium needles are described and tables given showing the details of the results. The action of the heat of boiling water is borne by radium preparations without any damage. The irradiation of radium needles with the usual filtration of 0.2–0.5 mm. platinum, which allows only the hard beta rays and the gamma rays to act, does not bring about sterilization of the surface. Alcohol and ether disinfection of the preparations is not always effective. The best method therefore of sterilizing radioactive preparations is in the boiling water bath or still better in flowing water vapor.—*Audrey G. Morgan.*

Rosenthal, Maurice, and Grace, Edwin J. Experimental radium poisoning. 1. Bone marrow and lymph-node changes in rabbits, produced by oral administration of radium sulphate. *Am. J. M. Sc.*, May, 1936, *191*, 607–618.

The author produced radium poisoning by the oral feeding of radium to rabbits. The results coincided with the observation made upon humans suffering from radium poisoning. Jaw necrosis and bone marrow changes consisting of early hyperplasia of the erythropoietic elements were followed by a decreased maturation of the erythroblasts and replacement of these elements by myelocytes. There developed myeloid tissue in the lymph nodes and spleen associated with extreme myelocytic hyperplasia in the marrow which resembled that found in the leukemia of roentgen-ray and radium workers.—*J. H. Harris.*

Lang, Gustav. Über die Permeabilität der menschlichen Haut für Radiumemanation im Luftbad. (The permeability of the human skin to radium emanations in the air-bath.) *Strahlentherapie*, 1935, *52*, 187–192.

Experiments are described in which the permeability of the human skin to radium emanations was tested. In previous experiments, emanations dissolved in water have been used but in this series gaseous emanations were

used. The subject was placed in a cabinet that could be closed air-tight. A measured amount of radium emanation was introduced into the cabinet. The patient breathed air free of emanation through a specially arranged valve and the total amount of expired air was measured in a rubber balloon.

The radium emanation in the expired air showed that the human skin is permeable to radium emanation though the air-bath in these cases contained a very low concentration of radium emanation.—*Audrey G. Morgan.*

PAGE, IRVINE H. Production of nephritis in dogs by roentgen rays. *Am. J. M. Sc.*, Feb., 1936, *101*, 251–256.

The results of other investigations in producing chronic nephritis by roentgen rays were confirmed by the author. The only point of interest in his experiments was that the kidneys were transplanted beneath the skin of the flank and then were given repeated small doses of radiation. The changes consist largely in tubular damage with usually less external glandular changes.—*J. H. Harris.*